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THE CLINICAL APPROACH TO THE RHEUMATIC PATIENT*

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THE program of this third meeting of the American Association for the Study and Control of Rheumatic Diseases is given over entirely to the diagnosis of rheumatic diseases. It has fallen to my lot to open the scientific session with a discussion of the clinical approach to the rheumatic patient. I have used the word "rheumatic" in preference to "arthritic" to emphasize the general nature of the problem and the necessity for a broad point of view in beginning the study of a patient with skeletal disease. It is vitally important that every clinician have a definite train of thought and method of examination when confronted with a patient suffering from rheumatic disease.

Some clinical grouping of the rheumatic diseases is necessary, as the patient must be placed in a provisional pigeonhole after the preliminary history and physical examination. This brings up the question of the classification of arthritis and related conditions, which has caused so much confusion in the past. It is hopeless to discuss the different classifications or the different terms used to indicate the same clinical type of pathologic process. A simple and most satisfactory way to approach the rheumatic patient is for the clinician to ask himself a series of questions. The first is whether the skeletal symptoms presented by the patient are due to articular or nonarticular disease. This question is usually easy to answer. The nonarticular rheumatic diseases include a variety of disorders having in common only skeletal involvement, such as myositis, neuritis, bursitis, and tenosynovitis and inflammation of the

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From the Cleveland Clinic.

connecting tissues around joints, muscles, and nerves. This group has been appropriately designated fibrositis, and thus separated off from those conditions showing actual joint involvement.

If the disease is a true arthritis, we ask:

1. Is it traumatic?
2. Is the joint disease a metastatic localization in the joint of bacteria of known fixed type from some focus?
3. Is the arthritis simply one manifestation of some general or constitutional disturbance as gout, hemophilia, tabes dorsalis, or the allergic state?
4. Is it rheumatic fever?
5. Is it rheumatoid arthritis of unknown etiology?
6. Is it primary osteoarthritis of unknown etiology?

If all such possibilities are kept in mind and the patient is examined and studied completely, these questions can usually be answered and the patient's disease thus placed in a definite category. The classification corresponding to these groups is given in the following table:

CLINICAL GROUPING OF ARTHRITIS

I. *Due to known cause:*
   1. Arthritis due to trauma.
   2. Specific infectious arthritis due to metastatic localization in joint of bacteria of fixed type (as gonococcus).
   3. Arthritis occurring as one manifestation of:
      a. Metabolic disturbance (as gout).
      b. Constitutional abnormality (as hemophilia).
      c. Neuropathic disorder (as tabes dorsalis, syringomyelia, or after a hemiplegia).
      d. Serum disease.

II. *Due to unknown or no specific cause:*
   1. Rheumatic fever.
   2. Rheumatoid (atrophic or proliferative) arthritis.
   3. Osteoarthritis (primary degenerative or hypertrophic arthritis).

The criteria used in differentiating the different types will be discussed in the papers to follow.

After having considered the possible clinical groupings of arthritis, the next question to answer is: What pathologic changes are taking place in the joint under study? Fortunately, there is no difference of opinion concerning the fundamental changes which are only two in number: (1) primary proliferation of synovial membrane and (2) primary degeneration of joint cartilage. These changes briefly summarized below must be visualized by the clinician.

PATHOLOGIC GROUPING OF ARTHRITIS

I. *Proliferative* characterized by primary proliferation of synovial membrane (thickening and infiltration of membrane followed by pannus formation, secondary erosion of cartilage and fibrous or bony ankylosis).

II. *Degenerative* characterized by primary degeneration of joint cartilage (splitting, softening and erosion of cartilage with secondary formations of bony spicules at joint margin).

The pathologic grouping does not correspond to the clinical grouping. Nichols and Richardson[1] made this clear in their original study of the pathology of chronic joint disease by stating that "each type represents reaction of the joint tissues to a considerable variety of causes." It is vitally necessary, however, in the management of a patient with joint disease to visualize the anatomic changes produced by the disease in and around the joint.

In the patient with joint disease of known etiology, it is apparent that the cause should be removed or treated to prevent its progress or further involvement. Influencing factors should be recognized and treated also, and the already damaged joint must be treated to return it as nearly as possible to normal. The group of joint diseases of known etiology present, however, such definite indications for study and treatment that there is little difficulty in determining the proper management of such cases.

Unfortunately, the group of arthritides of unknown etiology constitutes by far the majority of all cases of joint disease, and since by definition, the cause is unknown or nonspecific, the management is difficult. The cause cannot simply be searched for and removed or treated, and the damaged joint treated in an attempt to return it to as nearly a normal condition as possible, as we do with specific infectious, constitutional or traumatic arthritis. How then shall we approach such a patient? A very satisfactory procedure is to think of the joint disease in terms of *specific etiologic* factors and *influencing* factors. We have already stated that the specific etiologic factors are unknown or nonspecific, although it is quite generally agreed that such must be present and that the joint disease cannot develop without them. These factors are:

1. Infection with some unknown bacterium or filtrable virus in rheumatoid arthritis (atrophic, proliferative).

2. Ageing or disturbance in nutrition of cartilage in osteoarthritis (hypertrophic, degenerative arthritis).

Even if we do not know the specific organism directly responsible for rheumatoid arthritis and without which the disease cannot exist, there are numerous known factors which profoundly influence the causative organism and without which the specific organism might well produce no joint disease. Such influencing factors may be designated as *precipitating* factors and thought of as conditions which render the specific etiologic factor active. An excellent known analogy illustrating this point of view is herpes labialis which is due to a filtrable virus. This disease may be precipitated under numerous conditions such as: (a) a known bacterial infection as pneumococcus lobar pneumonia or meningitis due to the meningococcus; (b) certain protozoal infections as malaria; (c) exposure to cold; (d) artificial fever therapy; (e) digestive disturbances; (f) nonspecific protein injections as typhoid vaccine, and various other ways. Here we think of the virus immediately responsible for the disease as probably being constantly present in an inactive form in the tissues of the lip and rendered pathogenic by some secondary precipitating factor. Bland and Jones[2] have made similar observations in rheumatic fever.

The precipitating factors which must be considered in the study of rheumatoid arthritis are:

1. *Exposure to cold and damp:* This is a well-recognized relation and probably determines largely the greater incidence of rheumatic diseases in the colder climates.

2. *Specific infections,* as acute tonsillitis and dysentery. Infections by the streptococcus group are especially prone to excite arthritis just as certain bacterial infections are almost always accompanied by herpes labialis.

3. *Chronic focal infections,* especially in the teeth and tonsils.

4. *Undernutrition* causing a general lowering of resistance to all infections.

5. *Toxemia,* as from hyperthyroidism.

6. *Diminished blood flow* in the extremities due to a spasticity of the arterioles. This is primarily a disturbance of the nervous system producing the characteristic pale, cold, clammy, cyanotic extremities of the patient with rheumatoid arthritis.

7. *Exhaustion* from any cause.

Other factors might be cited. Alone or in combination, these factors may precipitate rheumatoid arthritis when the disease would not otherwise be active even if the specific etiologic organism were present. At times, the specific organism alone, however, may be sufficiently virulent to set up the disease in the absence of any precipitating or contributing factor.

While no person normally ever has rheumatoid arthritis every person, if he lives long enough, has at least some degree of osteoarthritis, since this form of arthritis is a manifestation of age, just as arteriosclerosis and gray hair are manifestations of the ageing of body tissues. If this conception be correct, there is no specific etiologic factor, such as a single microorganism, responsible for the disease any more than gray hair is due to a single causative factor.

Very frequently, the actual joint changes are all out of proportion to the changes normally to be expected from the chronologic age, or the condition may be much more painful than normal. Here the problem is to determine the factors which have accelerated the ageing process and thus made the physiologic age exceed the chronologic age. The more important accelerating factors are:

1. *Abnormal metabolism* as hypometabolism, diabetes, and gout. Hypometabolism is primarily a lowered rate of chemical activity of the body tissues. It is apparent that such a condition would influence adversely the nutrition of the joint cartilage. In gout, an excess of uric acid is deposited in the joint cartilage.

2. *Trauma* as from overuse, overweight, or abnormal stress from a mechanical defect as flat feet. Since the abnormal cartilage is softened, it is apparent that erosion is more rapid under such conditions.

3. *Disturbance in circulation,* as from arteriosclerosis, hypotension or hypertension.

4. *Toxemia from infection.*

5. *Nutritional deficiency* in which something necessary for the normal nutrition of joint tissues is lacking.

6. *Gastrointestinal disturbances,* as achlorhydria or constipation.

7. *Exhaustion* from any cause.

After all, a patient with arthritis presents himself to the physician for relief of his disability. The mere fact that the immediate etiologic factors are unknown or are not specific does not prevent much being done for the patient. The disease may be rendered inactive if precipitating and accelerating factors are searched for, treated, or removed. It is imperative then to study the patient with chronic arthritis from these different standpoints.

Every patient with this serious disease is entitled to a careful history, a thorough physical examination and a most complete laboratory study, and only after such a survey should treatment be instituted.

How shall we study a patient with rheumatoid arthritis or with osteoarthritis to uncover the precipitating and accelerating factors? A painstaking history often reveals the basis for a chronic exhaustion by reason of an inherited weakness of constitution or past illness, overwork, lack of rest or abnormal mental strain. The physical examination by reason of body build, general state of nutrition, blood pressure, apparent infection or nutritional deficiency may give additional data. We must depend on the laboratory for further information. The laboratory examinations of value are:

1. The sedimentation rate of the red corpuscles.
2. A detailed study of any anemia present. In rheumatoid arthritis, this is frequently a hypochromic anemia.
3. The glucose tolerance curve.
4. The blood uric acid.
5. The test meal.
6. Gastrointestinal x-ray study.
7. X-ray study of teeth and sinuses.
8. The basal metabolic rate.

SUMMARY

In approaching the clinical study of a patient with chronic arthritis we should:

1. Differentiate articular and nonarticular rheumatic disease.
2. Determine whether the arthritis belongs in one of the groups with known etiology or falls into the groups with no known or no specific etiology.
3. Visualize the pathologic changes occurring in and around the joint.
4. In rheumatic fever and rheumatoid arthritis where the etiology is unknown, search for precipitating factors.
5. In osteoarthritis, where there is no specific etiology, look for accelerating factors which speed up the normal ageing process.

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DIFFERENTIAL DIAGNOSIS OF ARTHRITIS FROM STANDPOINT OF PATHOLOGY*

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STRICTLY speaking the term "pathology" deals especially with "the structural and functional changes caused by disease." It is probable, therefore, that the pathology of arthritis consists of more than just the changes in the joint proper. Some of the changes which occur in the tissues other than those that go to make up the joint are known. In some of the joint diseases, however, even the exact pathology of the joint itself is not yet entirely clear. Furthermore, in describing the pathology of joint diseases, it is necessary to allow for various stages of the same process and for the secondary results of the primary involvement. I shall now try to review the pathology of some of the tissues in the more important types of joint disease, tuberculosis excepted.

Gout.—The condition known as gout has a long history and is one of the most interesting of medical diseases. It has long been presumed to be primarily a disorder of metabolism. The factors which induce the alleged metabolic disorder are not yet determined. There are, however, some factors which are believed to play a part in this change of metabolism. Among the more important of these are an hereditary predisposition, lead, and alcohol. None of these seem to account in all instances for the symptom-complex known by this name. Some of the changes of the tissues in gout are well known even though their interpretation is not clear. The newer chemical methods have demonstrated that in almost all instances there is an increase in the uric acid content of the blood in gout. Generally this persists during apparently inactive phases. Ordinarily the increase of the uric acid is not paralleled by the other protein constituents of the blood. The significance of the change, however, is uncertain, especially in view of the fact that some normal individuals show a uric acid content of the blood in excess of that occurring in gout. Furthermore, the highest values of blood uric acid which have been determined have been in cases of uremia and leucemia in which there have been no characteristic symptoms of gout. It is obvious therefore that further clarification of the significance of the high blood uric acid in gout is necessary. The second major tissue change which is known in gout consists in the deposit of urates in various tissues. There is to some extent an elective affinity for this precipitation to occur in the fibrous tissues, especially in those around the joints and in the lobes of the ear. In the later stages of the process the urates are deposited more widely and are especially conspicuous in the bone around some of the joints. When this precipitation occurs gradually little in the way of secondary manifestations seem to be pro-

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duced. When the precipitation occurs rapidly, marked secondary changes are set up. The most characteristic of such reactions is the inflammation which affects most of the tissues surrounding the area of deposit. Its clinical translation is pain, redness, and swelling, but with the exception of those few cases in which amputation has been mistakenly performed for the pain little is actually known of the microscopic picture at this stage. The same lack of knowledge applies to the inflammatory exudate in the joint which usually accompanies an acute attack.

Gonococcal Arthritis.—Arthritis due to the gonococcus is definitely a part of the picture of gonococcus infection. It must therefore be obvious that the present discussion be confined to the pathology of the joints alone. Whether there are two or more types of arthritis produced by the gonococcus is still a matter of debate. The conception that there are two or more types is based more on clinical grounds than on the known pathology. Certainly there is one type in which there is direct invasion of the joint tissues by the organism. Keefer and others have pointed out the involvement of the synovial membrane in at least one stage of this direct invasion. The membrane shows the characteristics of an inflammatory reaction. Under the superficial synovial cells there is a more or less localized infiltration of leucocytes, lymphocytes, and macrophages. It is probable that the relative proportions in which these cells are found are dependent on the acuteness and stage of the bacterial invasion. Accompanying the reaction in the synovial membrane there is usually an inflammatory exudate in the joint space. From this exudate gonococci can be occasionally isolated when careful technic is used. Inflammatory cells, especially leucocytes, are also generally present in large numbers. There is possibly another type of arthritis initiated by the gonococcus. Some investigators believe that this other type is a true sensitization of the joint tissues to the products of metabolism of the organism. In any case there seems to be a type of joint inflammation due to the gonococcus, but in which it is impossible to isolate the organisms, either from the exudate or the surrounding tissues. At present very little is known of the pathology of the synovial membrane under such circumstances. It is my opinion that the finding of large numbers of eosinophile cells either in the joint fluid or in the synovial membrane would do something to corroborate the conception of the existence of this disorder as a pathologic entity. Positive proof, however, will be very difficult.

Degenerative Arthritis.—I do not wish at this time to enter into the controversy concerning the causation of degenerative arthritis. Certainly the end-result which is recognized by this term is sufficiently characteristic to be relatively easily described. In the tissues other than the joints there has been no description of any constantly occurring lesions. It is true, however, that degenerative changes in other tissues often accompany those which appear in the joints. There may be considerable calcification of the cardiovascular system or there may be evidences of wear and tear in almost any portion of the body. The characteristic pathology in the joints has been adequately described by numerous investigators including Nichols and Richardson, Allison and Ghormley, Bauer, and Keefer. Thus Nichols and Richardson say: "The

joint cartilage is irregular in thickness, and markedly so in structure. It is fibrillated and calcified. Its cells are swollen. Parts of the cartilage may be ossified. The underlying bone is thickened and dense. The marrow is fatty and fibrous. The synovial membrane is thickened, fibrous, and is thrown into villi. Several observers have noted cyst formation in the bone in the region of the joint." To this description relatively little more needs to be added. The primary lesion seems to involve the articular cartilage, which when once injured has relatively little ability to return to its original state. As the mechanical process continues, the erosion and fragmentation of the cartilage become more marked and the defense mechanism offered by nature results in the subchondral bone becoming more dense and showing proliferation. If this proliferation progresses unchecked, portions of the bone may break off and form loose bodies in the joint space. The other changes which may also be observed seem to be essentially the result of this process. Thus the thickening of the synovial membrane and joint capsule, the increase in the vascular supply to the capsule, and the mild inflammatory reaction which is occasionally seen in the membrane can usually be explained on the basis of the increased trauma to the joint resulting from destruction of cartilage and proliferation of bone. When well established, therefore, nature has set up a train of defense reactions which it is later unable to halt.

Rheumatoid Arthritis.—In the tissues other than the joints and surrounding fibrous and muscular tissue, nothing absolutely characteristic has yet been described. It is probable that some reflection of the process exists in the blood, judging from the fairly constant deviations of the sedimentation rate. The exact nature of these changes is uncertain. Practically all competent investigators are agreed that the primary tissue affected in rheumatoid arthritis is the synovial membrane. It is also agreed that the lesion seen here is an inflammatory one. What has not been so clearly understood is that this inflammatory lesion is one in which in all probability certain definite stages can be recognized. The first stage probably consists of a somewhat diffuse proliferation of most of the membrane. The synovial cells remain essentially unaltered, but there is an increase in plasma cells, lymphocytes and probably sometimes in eosinophiles. As the condition progresses, but dependent partially on speed of the progress, there is an increase in the number of inflammatory cells in the synovia, especially lymphocytes and plasma cells. Polymorphonuclear leucocytes may appear either in the synovial tissue proper or in the lumen of the blood vessels. Sometimes the cellular infiltration may be perivascular, but it is not always so. Almost from the beginning there is a constant increase in the number of fibroblasts seen in the membrane. I believe that the pathologic picture varies depending on the course which the process takes in any one joint or portion of a joint. Thus in that condition in which the process continues unhalted by improvement the inflammatory appearance reaches a maximum, from which time with occasional exacerbations it is gradually replaced by fibrous tissue until no further sign of inflammation exists. It is this fibrous tissue replacement which produces the ankylosis which may later become cartilaginous or bony. In some joints a phase of resistance may

appear which is characterized pathologically by groups of lymphocytes and plasma cells quite definitely separated from an essentially normal though perhaps thickened synovial membrane.

It is very important to know whether the condition known as rheumatoid arthritis is a specific disease caused by a specific etiologic agent. The study of the pathology of this condition suggests but does not prove the specific nature of the process. It has been claimed that because a pathologic picture similar to that seen in some stages of rheumatoid arthritis in man can be produced in rabbits by nonspecific allergic inflammation, that rheumatoid arthritis is not a specific disease. While this may be true, it is necessary to bear in mind that Dr. Key has produced similar microscopic changes by injections of weak acids and weak alkalis, and quite independently I have also produced a picture in the synovia of rabbits, closely simulating one stage of human rheumatoid arthritis by injection of acetone or turpentine. As a rule, however, there seems to be no question but that the major forms of arthritis when typical can be clearly differentiated on the basis of the characteristic pathologic picture which they produce.

DISCUSSION

DR. M. HENRY DAWSON, NEW YORK, N. Y.—Dr. Jordan has given us a very complete résumé of the morphologic changes in the various forms of chronic arthritis. I do not propose to comment to any extent on the observations which he has made on the pathology of gout and gonococcal arthritis. The morphologic pathology of these two diseases has been studied in detail and is now well understood. For a detailed description of the tissue changes in gout the monograph of Professor Pommer (Innsbruck) should be consulted. The pathology of gonococcal arthritis is also reasonably well known. It manifests the characteristics of an acute, subacute or chronic suppurative inflammation. When it comes to the pathologic changes in rheumatoid and osteoarthritis the situation is not quite so clear. However, if one reads the literature carefully, one finds that many detailed and excellent investigations have been made on the pathology of these two forms of arthritis. One of the earliest and best descriptions was that of Hoffa and Wollenberg in 1908. For some reason this work does not seem to be widely known in America. A year later Nichols and Richardson published their classical monograph. In 1926 Heine published his monumental study on the relationship between age-period changes and degenerative arthritis. In his investigation Heine examined tens of thousands of joints in the course of 1,002 autopsies. Among other valuable contributions have been the studies of Allison and Ghormley, Timbrell Fisher, Klinge and his associates, and many other more recent investigators. The one inescapable conclusion from all these studies is that rheumatoid and osteoarthritis represent two totally different pathologic processes. Rheumatoid arthritis is an inflammatory process related in some very intimate way with infection. Osteoarthritis is an age-period, degenerative disease not associated with infection in any direct manner. Pathologically the distinction between rheumatoid arthritis and osteoarthritis is quite as sharp and well defined as that which exists between syphilitic aortitis and arteriosclerosis.

In this connection I should like to make brief reference to the contrary opinion expressed by Knaggs. Originally Knaggs believed that the two diseases under discussion were distinct entities, but after studying the Strangeways collection of joints he arrived at a different conclusion. I believe that this contrary point of view can be explained by the fact that the material studied consisted largely of old and "burnt-out" specimens of the two diseases. It is well known that secondary degenerative changes are frequently superimposed upon rheumatoid arthritis. It is further well recognized that degenerative arthritis is an extremely common event, especially in the later decades of life. It is therefore not

surprising that in certain cases the changes of the two diseases should coexist in the same patient and even in the same joint. Such observations cannot be construed as evidence in favor of a relationship between the two conditions.

So far as the specificity of the synovial lesions in rheumatoid arthritis is concerned one is reminded of the controversy over the specificity of the Aschoff body in rheumatic fever. This question has not yet been finally answered but the majority opinion favors the theory of a specific lesion. Although there is considerable evidence indicating that the synovial changes in rheumatoid arthritis are also specific, it is not yet possible to express a final opinion.

I should like to make one other comment concerning the pathology of rheumatoid arthritis and that is in regard to the subcutaneous nodule. To my mind this constitutes the most characteristic lesion in the disease. It is frequently possible to make a positive diagnosis from the histologic appearance of the nodule alone. It is true that only 15 to 20 per cent of patients with rheumatoid arthritis show these nodules but when found they are pathognomonic. They are never seen in osteoarthritis.

DR. PHILIP S. HENCH, ROCHESTER, MINN.—Since there is no one clinical or laboratory feature pathognomonic of atrophic arthritis, it would be very helpful in diagnosis if there were at least a specific pathologic lesion. Allison and Ghormley believed that the nodular collections of round cells which they described, seen in synovia and epiphyseal bone, are specific for atrophic arthritis. Somewhat similar collections were described by Timbrell Fisher, who recently spoke of them, however, as being "perivascular." Allison and Ghormley did not consider them perivascular, and Ghormley's recent studies with Deacon confirms this viewpoint. May I ask Dr. Jordan how he would describe them?

I cannot agree with Dr. Dawson that subcutaneous fibrous nodules are only seen in atrophic arthritis. As Dr. Slocumb will demonstrate later in this program, we have seen numerous subcutaneous nodules in many cases of fibrositis in which even after years of the disease arthritis has never developed.

DR. J. ALBERT KEY, ST. LOUIS, MO.—The synovial lining cells are connective tissue cells. Twenty-four hours after the joint is irritated these cells are changed and an osteoarthritic joint is often irritated.

As regards a clear-cut distinction between osteoarthritis and rheumatoid arthritis, the more one studies the synovial membrane of osteoarthritis, the less one will believe that such a distinction exists. It has been the custom since osteoarthritis was first found to begin in the cartilage, and that was a long time ago, to concentrate on the cartilage and bone, and also nothing has been done on the changes in the synovial membrane of osteoarthritis. For many years the orthopedic men have recognized a villous arthritis. The men interested in arthritis have said that such a condition does not exist.

In following cases of osteoarthritis I am more and more impressed with the fact that an individual may have marked degenerative changes in the joint over a period of many years and have no clinical symptoms. Then something may happen and the joint gets hot, filled with exudate and becomes a very acute joint. That joint is bound to have inflammatory changes in the synovial membrane. According to Dr. Dawson, that is a burned-out rheumatoid arthritis which has developed compensatory changes as a result of degeneration of the cartilage. On the other hand, I am perfectly sure in my own mind that it is chronic inflammation in an osteoarthritic joint. And I have seen numerous specimens on which I have operated in which there were marked inflammatory changes in the synovial membrane. I do not know the origin of rheumatic nodules, but I have never seen the pathologic picture such as Dr. Dawson described in rheumatoid arthritis presented by any other condition. I have excised some of these nodules, and I was totally unable to explain how they came about. I have always felt that the nodules of small round cells described by Ghormley and Allison are by no means constant in the synovial membrane of rheumatoid arthritis. It is only in old cases that they may be found and it is my experience that they are not perivascular.

DR. EDWIN P. JORDAN, CHICAGO (closing).—I do not know whether the aggregations of cells are perivascular or not, but I think most of them are not, at least from the evidence I have. I have been able to find blood vessels going through them in only a relatively small percentage of the total number. In a way, I think it is a relatively unimportant aspect of the subject.

With regard to the pathologic differentiation between degenerative arthritis and rheumatoid arthritis, everyone who has any opinion on that subject at all feels very strongly about it. There seems to be no middle point of view. Actually, I think that the end-result of the two processes in their pure form, if there is a pure form and there seems to be, is decidedly distinct pathologically. On the other hand, I do not personally see as sharp a distinction between the processes when applied clinically. In other words, in many instances the two seem to be intertwined in the one patient to such an extent that it is very difficult to draw any hard and fast line between them. The amount of synovial membrane involvement in what is supposed to be degenerative arthritis is sometimes almost as much as in rheumatoid arthritis. The inflammatory reaction may be fairly acute. It may be due in this instance to trauma from the bone rather than from infection. It may not be infection in rheumatoid arthritis, and hence it is exceedingly difficult to say in all instances during life, at least pathologically, that the process is one or the other. In some instances it is possible to differentiate with some certainty.

THE BRITISH ACTIVITIES FOR THE CONTROL OF RHEUMATISM*

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I WAS under the impression before I came over that among the activities at Kansas City there would be a group meeting to discuss the control of rheumatism in the largest sense of that word. I find myself with some alarm and trepidation faced with a program that makes it appear to me that you are engaged in the study of rheumatic diseases from the clinical and pathologic side. I got a little comfort from hearing Dr. Boots say that some of the etiologic factors in rheumatoid arthritis are not yet certain, but he took that comfort away from me by saying that we all know about osteoarthritis. My critical faculty came to my aid; things might happen in the calf that do not happen in the human being.

I am Chairman of the National Society for the Control of Arthritis in Great Britain. Of course it is concerned with the study and control of rheumatism but not primarily. It is not based primarily upon study of symptomatology found in all rheumatic problems. We have, as you know, in Great Britain a great deal of rheumatism of a disabling type. We have a great deal of disabling rheumatism to which we cannot as yet give any names, but which we would be very glad to catalogue. It has been definitely established through the Ministry of Health that there are more working hours wasted in Great Britain through conditions that are labeled chronic rheumatism, fibrositis, arthritis of indefinite origin, etc., than in any other disease. So nine years ago there was an effort to form a committee which would consist of doctors, industrialists, men of intelligence and foresight, who were aware that this was a big economic problem, and the Minister of Health. That committee was aborted because it began at a time when we, like you and like most other countries, were faced with domestic economic problems of such dimension that we could not see our way to get the necessary funds to run this committee. So we suspended our activities even before we began them. We waited until the spirit of optimism with which we British get inspired would enable us to function a second time.

We have done very little work up to the present. We have got a good deal of helpful recognition from the official government headquarters, that is the Minister of Health, and from the captains of industry. We have succeeded up to the date of my leaving London in collecting about one-third of the quarter million dollars that we aimed at getting in order to give this thing a proper trial. Our central committee at present is entirely medical. We hold, as I think most of you do over here, that if you really want an organization of the type that I am outlining, to succeed, to do good work

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and to keep straight, it must be essentially medical. I notice that we have as you have all sorts of groups which are not controlled by medical men and women. They are both free countries and if a few people get together and want to do something, there is nothing in our law, and probably not in yours, to prevent them from doing it. We really have an extremely good organization with the triad that I spoke of, medicine, the government in the person of the Minister of Health, and the industrial magnets. What we propose is that as soon as we are not likely to be aborted a second time, because we have not yet gone publicly for appeals, our committee will become an advisory scientific committee to organizations. We hold that it is better to get a decently large fund and then to go to the public for smaller donations. We then can incorporate as a National Campaign Against Rheumatism.

We have a precedent that I have been very interested in from its inception. I think everyone agrees that we have done exceedingly good work by concentrating a great deal of the diffuse and futile effort that was being made in study, research and therapy in the educational campaigns connected with cancer. We have on our scientific advisory committee representatives of medicine, government, and industry, which will give us freedom as to our material, and a most recent and approved association.

Our activities will be, first of all, a study of the various aspects of the rheumatic problem, including what we still call rheumatic fever. We shall have a research committee, because we will have money with which to subsidize research; just as our cancer campaign subsidizes both full- and part-time men, with researches of six months, twelve months, and up to five years, so we propose to do the same with the various group problems connected with chronic rheumatism.

With regard to treatment, we are still affiliated with the Red Cross Rheumatic Clinic, which is doing very good work in London and has two branches in the Province. Here all the physiotherapeutic measures which are so important to these chronic cases are available for the use of any patient sent in by members of the advisory committee or any one who is intrusted to him by a medical man. We expect naturally to increase the number of these rheumatism clinics, and we also have a scheme for studying more intensively some of the cases of the rheumatoid group particularly. So we will have a service for special research work and out-patient clinics for the more routine therapy. Then we have, as you have, spas, so-called sanatoria and watering places for the treatment of chronic rheumatic conditions. We have them represented on our medical committee, and they sent us fourteen representatives.

That is roughly what we are doing. You have apparently preceded us by about three years, so your optimism is a little ahead of ours. I want to bring greetings from the British Committee of which I have the honor to be the Chairman, and I would like to take back word that this group of distinguished workers in the rheumatic problem are representatives of the American group for the control of rheumatism.

THE ESSENTIAL FEATURES IN THE DIFFERENTIAL DIAGNOSIS OF RHEUMATOID AND OSTEOARTHRITIS*

RALPH H. BOOTS, M.D., NEW YORK, N. Y.

ALTHOUGH numerous authors since 1907 have described rheumatoid and osteoarthritis as entirely separate and distinct diseases this distinction certainly was not held by the majority of the medical profession, especially among those in this country. This was largely due to the obscurity of their etiology and to the confusion of their terminology.

Recently this clinical differentiation has been confirmed by the laboratory, and there has appeared a renewed interest in it, resulting in a more general acceptance of this view. There would now seem to be no further excuse to look upon these cases as examples of a single disease. It is most important that practicing physicians should recognize this, since numerically these two groups account for approximately two-thirds of all chronic arthritis patients, and there is a great difference in their prognosis and treatment.

The first of these, rheumatoid arthritis, represents a multiple arthritis which seems to be part of a response to a generalized infectious process. The second, osteoarthritis, is essentially a degenerative process involving joint structures at a time of life when other degenerative changes occur. This type does not present the picture of infection as does the first. The patient is nearly always middle-aged or elderly, and the joint lesions are probably as much a phase of senescence as the graying of the hair. Historically, they are very interesting. According to a recent review by Joseph Miller,[1] not a single instance of rheumatoid arthritis of the extremities is noted in 35,000 Egyptian mummies, carefully examined for evidence of disease; while practically every adult skeleton showed osteoarthritis of the spine.

With typical examples of these two conditions, the diagnosis presents no serious difficulty. The picture which comes quickly to one's mind of rheumatoid arthritis is that of a young adult, chronically sick, usually female, thin, anemic, with symmetrical spindle-shaped swelling of joints, perhaps with some psoriasis or subcutaneous nodules. With osteoarthritis the usual picture is that of a well-nourished, healthy-looking adult, past middle age, who feels well except for his rheumatism. Perhaps he walks with a limp. Many patients who show osteoarthritis by x-ray have no symptoms. With the exception of the distal joints of the fingers (Heberden's nodes), the joints involved are most frequently weight-bearing, i.e., the spine, hips, and knees.

Usually, however, this distinction is not so simple, and careful, extended examinations and observations over a period of time are necessary before one can be certain of the diagnosis. Rheumatoid arthritis may occur in the eld-

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erly, and the patient may not be anemic, thin, and the joints involved may not be symmetrical. Also, osteoarthritis may occur in thin, anemic adults. The diagnosis is equally difficult in very early cases of rheumatoid arthritis, before typical fusiform fingers develop and before the streptococcus agglutination test becomes positive and roentgenographic changes occur. Further complication is added when osteoarthritis is superimposed later in life on an already existing rheumatoid arthritis, or vice versa. A diagnosis should not be made on one feature alone, but only after a careful study of the patient and viewing the entire picture.

The following case histories are of two patients observed over a period of six years and illustrate some of the differences in the findings and course of the two diseases:

CASE 1.—(1931.) Female, aged thirty-two years. *Chief complaints:* Mild, general stiffness, especially of hands and feet, of six months' duration. Recently slight, painful swelling of fingers. *Family history:* Mother, father, and two sisters living and well. One sister had rheumatic fever as a child.

Physical examination: Height, 5 feet 6 inches. Weight 115 pounds. Blood pressure 120/80. Hands clammy; redness of thenar and hypothenar eminences. Slight fusiform swellings of fingers, due to soft swelling of proximal interphalangeal joints. Fingers and left shoulder slightly tender. Several psoriatic lesions over right thigh. Granular pharyngitis. Right antrum dark. No pus on irrigation. Tonsils removed in 1920. Heart: rate 80; no organic lesions.

Laboratory examination: W.B.C. 10,500; R.B.C. 4,500,000; Hg 80 per cent; sedimentation rate 15 mm.; uric acid 4.0 mg.; Strep. agg. 1:160, dil. (weakly positive). X-rays show slight general decalcification.

Diagnosis: Probably early rheumatoid arthritis.

Very little, if any, change in 1932 and 1933. W.B.C. 9,500; R.B.C. 4,000,000; Hg 75 per cent.

In 1934 she was abroad for three months. Had bad cold while abroad. Returned in November with increased joint involvement. Fusiform fingers more marked. Fluid in both knees. Muscle atrophy of thighs and hands. Shoulder and elbows stiff. Subcutaneous nodule 1 inch below right elbow. Temperature: 98°-99.4°; W.B.C. 12,500; Hg. 75 per cent. Sed. rate: 80 mm. Strep. agg.: 1:640; definitely positive. Psoriasis: very little change. X-rays show general decalcification. Most marked in joints involved. Soft tissue swelling. Narrowing of joint spaces of several phalangeal joints.

Treatment: Bed. Transfusions. Cod liver oil. Aspirin.

Diagnosis: Severe rheumatoid arthritis.

In 1935 she showed slow improvement. Up eight hours a day. Mild discomfort. Weight: 135 pounds. Sed. rate: 40 mm. Fingers still fusiform and a little stiff.

She spent the winter of 1936 in Florida. Afternoon rest. Weight: 140 pounds. Cod liver oil and occasional aspirin. Occasional periods of joint stiffness. Sed. rate: 32 mm.

CASE 2.—(1931.) Female, aged sixty years. *Chief complaints:* Discomfort in back, right hip and both knees, of four years' duration. History of fall six years ago and believes this caused her arthritis. *Family history:* Mother and father both had arthritis late in life.

Physical examination: Height: 5 feet 7 inches. Weight: 212 pounds. Blood pressure 170/90. Healthy-looking woman except for slight limp. Joints: painless bony swellings of distal finger joints; Heberden's nodes. Knees creak and are slightly swollen.

Laboratory examination: W.B.C. 6,000; R.B.C. 5,000,000; Hg 90 per cent. Basal metabolism -20 per cent; Sed. rate 25 mm. Strep. agg. negative. X-rays show hypertrophic changes in fingers and spine and both knees. Malum coxae senile of right hip. Bony density normal for her age.

TABLE I

	RHEUMATOID ARTHRITIS	OSTEOARTHRITIS
	Atrophic arthritis Proliferative arthritis Chronic infectious arthritis	Hypertrophic arthritis Degenerative arthritis Menopausal arthritis Senile arthritis
	Clinical Differentiation	
Geographic distribution	Most common in temperate climates; rare in the tropics.	Climate not much of a factor.
Family history	Usually a history of rheumatic fever or rheumatoid arthritis in an immediate member of family.	Frequently a history of a similar form of arthritis in one or both parents.
Past history	Occasionally a history of rheumatic fever; frequently of tonsillitis or sinusitis.	Not characteristic; sometimes a history of trauma or faulty body mechanics.
Age at onset	Any age; over 80 per cent between twenty and fifty.	Rare before 40. In women most common at menopause (menopausal arthritis).
Mode of onset	Rarely acute; usually subacute or insidious; often accompanied by migratory pains.	Insidious; not accompanied by migratory pains.
Patient's general condition	Usually undernourished, anemic, and "chronically ill." Frequently slight fever (99) and slight leucocytosis.	Well nourished, frequently obese; not anemic. No fever, no leucocytosis.
Joint involvement	Symmetrical and generalized; proximal interphalangeal joints especially involved.	Usually weight-bearing joints, spine, hips, knees. Exception, distal joints of fingers, Heberden's nodes.
Appearance of joints	Early: Periarticular swelling, fusiform fingers. Late: Ankylosis, extreme deformity, ulnar deflection.	Early: Slight articular enlargement. Late: More pronounced articular enlargement; ankylosis slight and never complete: Heberden's nodes.
Muscular atrophy	Often marked, particularly in later stages.	Not characteristic.
Cutaneous changes	(1) Extremities frequently cold and clammy; skin atrophic and glossy; redness of thenar and hypothenar eminences. (2) Psoriasis occasionally present.	No characteristic features.
Subcutaneous nodules	Present in 15-20 per cent of cases	Not present.
	Laboratory Differentiation	
Agglutination reaction with hemolytic streptococci	Positive in over 50 per cent of typical cases.	Never definitely positive.
Sedimentation rate	Usually greatly increased; tends to return to normal as patient improves.	Normal or only slightly increased.
Roentgenologic findings	Early: Osteoporosis, periarticular swelling and joint effusion. Late: Narrowing of joint space, bone destruction, ankylosis, and deformities.	Early: No osteoporosis; slight lipping at joint margins. Late: Marked lipping, osteophytes.

Diagnosis: Osteoarthritis. Obesity. Hypothyroidism.

Treatment: Low calorie diet. Thyroid. Physical therapy. Rest periods.

In 1936 the patient had been seen occasionally since 1931. Fairly comfortable. Weight: 170 pounds. Basal metabolism −7 per cent. Taking thyroid, two grains a day.

Laboratory examination: W.B.C. 5,000; Hg 85 per cent; Sed. rate 20 mm. Strep. agg. negative. X-rays showed slight increase in hypertrophic changes as compared with 1931.

It is rate that all of the pathologic findings of either disease are presented by any given patient. For the sake of conciseness, the essential features in the differential diagnosis, both from clinical and laboratory standpoints, are arranged in tabular form. This is a revision of a tabulation published by Dawson, Sia and Boots in 1930.[2]

HEMOLYTIC STREPTOCOCCAL AGGLUTININS

Perhaps the most significant laboratory finding is the presence of streptococcal aggutinins in the blood serums of patients with rheumatoid arthritis. These are never present in the blood serums of patients with osteoarthritis. They were first reported by Cecil, Nicholls, and Stainsby in 1931[3] and this work has been confirmed by other workers including Dawson, Olmstead and Boots,[4] McEwen, Alexander, and Bunim[5] and others.

SEDIMENTATION RATE OF THE ERYTHROCYTES

The determination of the sedimentation rate of the erythrocytes is now a routine procedure in all arthritis clinics. In our clinic we use the Westergren modification of Fahraeus' technic. It is not only of assistance in diagnosis, but offers a convenient method of following the degree of activity of any type of infectious arthritis. Particularly is it useful in evaluating the results of the therapeutic measures employed. In active cases of rheumatoid arthritis, the sedimentation rate of the red blood cells is, as a rule, greatly elevated, usually attaining values exceeding 30 mm. in one hour. The rate parallels to an extraordinary degree the severity and extent of the arthritic process; as the patient becomes worse, the rate increases, and with improvement, it tends to return to a normal value. On the other hand, in cases of osteoarthritis, the sedimentation rate, while occasionally slightly elevated, rarely attains values greater than 20 or 30 mm. in one hour. Their value in this test is comparable to that of leucocyte curves in certain other diseases, leucocyte counts being of very little practical value in these diseases.

BLOOD CHOLESTEROL DETERMINATION

Studies recently made by Hartung and Bruger,[6] as well as Key,[7] show that the plasma cholesterol tends to be low in rheumatoid and high in osteoarthritis. It is definitely known that an increased blood cholesterol occurs in the aged, but Hartung believes that the readings which he has observed in osteoarthritis are higher than can be accounted for by age alone. Also, Hartung and other observers have found an elevation of the nonfilamented polyneutrophiles in rheumatoid arthritis, with a normal count of these cells in osteoarthritis. This suggests an infectious origin of the former.

ROENTGENOGRAPHIC FINDINGS

Roentgenograms are of great importance in making a differentiation between rheumatoid and osteoarthritis. Various authors have reported that the x-ray pictures of these two conditions are quite distinctive.

ETIOLOGY

It is interesting to speculate on etiology. Just as the clinical and laboratory findings differ, it seems quite plausible that there should be a difference here. Although it must be stated that the direct etiology of rheumatoid arthritis is not definitely known, it is difficult to escape the conclusion that it is an infectious disease. The agglutination reaction suggests that it is connected in some way with *Streptococcus hemolyticus* infection. Other factors, such as heredity, environment, avitaminosis, faulty metabolism, or psychic trauma, may also play a part.

The explanation of the cause of osteoarthritis seems more clear, especially since the recent work of Bennett and Bauer.[8] He found, in autopsies of human knees at different age periods of life, that with each succeeding decade beyond the second, the knee joints showed increased pathologic changes, degenerative in nature and indistinguishable from those characteristic of osteoarthritis. His examination of the knee joints of cattle at different age periods suggests that trauma plays a definite part in etiology. Pemberton,[9] by experimental interference with the vascular supply to the patellae of dogs, was able to produce hypertrophic changes, indicating that altered blood supply might be partly responsible. There seems to be no specific etiology. A number of factors may contribute, and it might be possible that osteoarthritis is due to the summation of joint insults during the entire time of one's life.

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DIFFERENTIAL DIAGNOSIS BETWEEN STRÜMPELL-MARIE DISEASE AND OSTEOARTHRITIS OF THE SPINE*

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THE anatomic changes of Strümpell-Marie disease were described more than one hundred years ago. Bechterew in 1893 described the clinical signs and symptoms of a disease that differed only from the classical description by the presence of certain symptoms which he thought were due to spinal cord injury. Strümpell in 1897 reported 3 cases which he designated as chronic ankylosing spondylitis. He was the first to suggest that the disease was infective in character. The following year Marie reported 5 cases. Joel Goldthwait in 1899 described 10 cases. He expressed the opinion that etiologically the disease was trophic in origin. The earliest complete account, however, was made by Fraenkel in 1904. He coined the term "spondylitis ankylopoietica." The first noteworthy contribution in America was made by G. R. Elliot of New York City in 1905. He gave a very accurate clinical description and described the pathologic findings. He reported 5 cases, 4 of which he thought were due to gonorrhea and not associated with rheumatic disease of the extremities. The fifth case was associated with rheumatoid arthritis.

Pathology and Etiology of Ankylosing Spondylitis.—This disease may develop as a complication of a number of infective diseases, one of which is rheumatoid arthritis. Rheumatoid arthritis of the extremities begins in the synovial membrane; at least it is here that there is evidence of an inflammatory process. The only synovial membrane in the spine is in the small lateral articulation of the transverse processes and the ribs, usually referred to as the small articulations of the spine. It is generally believed, although not conclusively proved, that these articulations are first involved in this disease. There is a marked tendency for early ankylosis. If this occurs in the dorsal spine, the thorax becomes immobilized. Associated with this ankylosis (and some claim even earlier than it), there is osteoporosis in the adjacent vertebrae. It appears improbable that the atrophic changes in the vertebrae precede the anklyosis of the small articulations. Further pathologic changes develop only after the lapse of years, as the disease is chronically progressive in character. Patients dying of some intercurrent disease may show only the changes already described.

The later changes are ossification of the intervertebral ligaments, especially the anterior longitudinal ligament. There may be ossification of the periphery of the intervertebral disc, and extension of the spongiosa of the vertebra through the central portion of the disc. If the pathologic changes are completed, the involved spine structurally resembles a long bone. Without regard to the nature of the infective agent, the pathologic changes are identical. This

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disease is infective in character and unlike rheumatoid arthritis of the extremities may be produced by a variety of microorganisms and develop as a complication of various diseases, as rheumatoid arthritis, gonorrhea, typhoid fever, bacillary dysentery, and influenza. One case has been reported after undulant fever. In Anton Fischer's 100 cases of ankylosing spondylitis, 29 patients had rheumatoid arthritis of the extremities. In reply to my letter of inquiry regarding the nature of these joint changes, he replied that they were what the English call rheumatoid arthritis. It is of interest to know that all writers on this subject refer to the previous history of acute rheumatic fever in many of these patients. The involvement of the extremities may precede or follow the spinal disease. The course of the disease is extremely variable. Its progress is always very gradual. Remissions of rather long duration have been reported. Its course resembles that of rheumatoid arthritis. The disease is rare in women; all of Fischer's 100 patients were males. It is claimed that in Germany the disease became more prevalent following the War. In certain veteran hospitals in this country many cases were found. This increase can probably be accounted for by the greater incidence of various infections. Marie believed that trauma played an important rôle. This idea has been abandoned. There is no evidence that heredity plays a rôle.

Pathology and Etiology of Spinal Osteoarthritis.—The spine of man has not become adapted to the erect posture. The excessive pressure sustained by the intervertebral discs leads to deterioration. The discs lose their resiliency and become somewhat thinner. As a consequence of this change, the mobility of the vertebra is increased as its fixation is dependent to some degree on the intervertebral disc. The increased mobility results in greater strain on the intervertebral ligaments. These ligaments enter the periosteum of the vertebra just adjacent to the vertebral rim. The irritation of the periosteum leads to the formation of osteophytes along the course of the ligamentous attachment. Traction is the chief factor in osteoarthritis of the spine. Pressure with destruction of cartilage is the most important factor in osteoarthritis of the extremities. Osteoarthritis is a degenerative disease.

Signs and Symptoms of Ankylosing Spondylitis.—The fact that the disease begins in the small articulations of the spine and the proximity of the spinal nerves to this region accounts for the severe root pains in this disease. It is believed the nerve is directly involved in the inflammatory process. Root pain in the acute cases is the outstanding symptom. If the cervical spine is involved, numbness, and transitory paralysis in the arms have been reported. In case the lumbar spine is involved (and it is in this region that the disease usually begins), numbness and loss of power have been noted in the legs. The acute inflammation in the small articulations of the dorsal region may immobilize the ribs long before actual ankylosis has developed. The breathing then becomes abdominal. The thorax was immobilized in all but one of Fischer's 100 patients. The degree of pain the patient experiences depends on the acuteness of the inflammatory process. In case the onset is very gradual, the patient's chief complaint is stiffness in the back. Effort on bending, especially laterally, is usually slightly painful. Sudden pressure on the shoulder or a jar may excite some pain. There is slowly increasing rigidity of the

back until the patient finally develops a poker spine. The patient gradually develops a kyphosis with absence of the normal lordosis. In the early stage of the disease, there may be marked spasticity of the spinal muscles. With this there may be marked tenderness to pressure lateral to the spine. Tapping the spinous processes may excite pain. Eventually the chest becomes flattened and the anterior posterior diameter lessened. In the advanced stage the patient assumes a characteristic appearance when walking. If the cervical spine is involved, the head is immobile and is held either erect or markedly bent forward; the chin may almost rest on the sternum. He stoops on account of the kyphosis. The gait is slow and shuffling.

In addition to the spinal involvement, some patients have rheumatic involvement of the various articulations in the body. The hip and shoulder are most frequently involved. Geilinger has summarized from available sources the incidence of ankylosis of the various articulations. The hip is involved in 61 per cent, shoulder 58 per cent, knee 44 per cent, foot 41 per cent, finger 19 per cent, hand 18 per cent, elbow 17 per cent, and jaw 17 per cent. When details are discussed, it appears doubtful if there is true ankylosis of the shoulder. Repeatedly reference is made to inability to abduct the arm beyond the horizontal. In no instance have I been able to obtain definite evidence that the shoulder is ankylosed. The inability to abduct completely could be explained by spasm of the abductors due to involvement of the brachial plexus. The literature, as far as I could determine, does not contain information as to whether or not involvement of the shoulder is always associated with ankylosing spondylitis of the cervical spine. In the hip there is true ankylosis. There are two references to investigations in which the pathology of the hip has been studied. Fraenkel reports that the ankylosis is bony in type. Buckley describes it more in detail: "There is early limitation of motion due to ossification of the fibrocartilage around the rim of the acetabulum. A similar bony collar develops around the femur at the margin of the articular cartilage. These changes eventually prevent movement of the articulation." These findings are those of osteoarthritis of the hip. The factors are present that predispose to osteoarthritis, that is, change in posture due to the absence of normal lordosis and ankylosis of the lumbar spine. It is not unusual in rheumatoid arthritis of the foot to find osteoarthritis of the knee which is probably caused by a disturbance of posture which produces unequal pressure on the joint surface.

X-ray is a great aid in the diagnosing of ankylosing spondylitis. The outstanding and easily recognized change is osteoporosis of the involved vertebrae. This appears very early. Obliteration of the interarticular space in the lateral articulations is not easily demonstrated, even in cases where the ribs are ankylosed. An exception to this can be made when the cervical spine is involved. Fischer reported that x-ray showed obliteration of the interarticular space in only 22 per cent of his cases. In advanced cases ossification of the ligaments and intervertebral discs can be demonstrated. The ligamentous ossification shows as a round smooth bulging at the level of the disc, giving a bamboo-stick appearance. The form of this bulging is quite different from that produced by fusion of osteophytes. Osteophytes are not present in

ankylosing spondylitis, except occasionally in patients where the disease develops late in life and in whom preformed osteophytes may be found.

Signs and Symptoms of Spinal Osteoarthritis.—According to Schmorl, osteophytes are found in 93 per cent of individuals in the sixth decade. It is evident that a very small percentage of people with this disease are aware of its presence. When symptoms are present, they take the form of root pains or neuralgia. These pains are rarely, if ever, so intense as those caused by ankylosing spondylitis. The cause of these root pains is still a debated question. Fischer is very positive that they are not directly due to the osteophytes. This disease may disable for certain occupations, as, for instance, mining and heavy lifting. It is generally an annoying, rather than a disabling, disease.

It is not necessary to discuss the x-ray findings in this disease, except to say that osteoporosis of the vertebrae is not present.

Differential diagnosis is rarely difficult. Ankylosing spondylitis in 60 per cent of the cases develops before the age of forty. Osteoarthritis of the spine becomes more frequent with advancing years. Ankylosing spondylitis is rare in women. Osteoarthritis is equally prevalent in both sexes. The sedimentation test is negative in osteoarthritis. Ankylosis of the ribs or rigidity of the spine does not occur in osteoarthritis. The difference in x-ray findings has already been dicussed. Fusion of osteophytes might offer some difficulty. Actual fusion of osteophytes over a considerable length of the spine is rarely observed.

DISCUSSION

DR. RUSSELL L. CECIL, NEW YORK, N. Y.—The beautiful photographs which Dr. Boots and Dr. Miller have shown certainly should convince us that there are two distinct types of chronic arthritis. We believe it helps us to think of the rheumatic type as an inflammatory disease and the other type as a degenerative disease; the former associated with inflammation, soft tissue swelling, exudate and fluid; and the latter with bony change, no soft tissue swelling, and absence of active inflammatory changes—a dry, creaking joint. One thing that confuses us is the fact that some of these patients with hypertrophic arthritis can go on so long without any pain and then suddenly develop pain. I believe Osgood is right when he says that in hypertrophic arthritis the pain is due in many cases to trauma, that is, the effect which these bony spurs have on the synovial membrane. If this mechanical irritation is sufficient we can get a hydrops in the joint or a villous arthritis, and still we are a long way from having the typical picture which we see in the infectious joint. Of course, there is no reason why the middle-aged patient should not get infectious or rheumatoid arthritis, and they do get it. I recently saw an old gentleman, seventy-seven years old, who was having his first typical attack of rheumatoid arthritis, with the characteristic fusiform fingers. Theoretically there is nothing to prevent an elderly lady from getting gonorrheal arthritis. She may already have marked hypertrophic arthritis. You may have Heberden's nodes on the distal phalangeal joints of the fingers, and fusiform swellings of the proximal phalangeal joints. Let us not forget that any irritant, if it is sustained, will produce hypertrophic changes in the bone. That does not have to be trauma, though trauma is a very common cause of it. We see it after fractures. We see it in joints containing foreign bodies. We see it after infection, and we see it in the Charcot joint and in gout. Some of the pictures shown here showed hypertrophic changes in the bone following long-standing infectious arthritis. If we have a patient, particularly in beginning middle age, who develops rheumatoid arthritis, it is perfectly natural, with the tendency toward osteal changes and cartilaginous degeneration, that with the development of rheumatoid arthritis there will be certain secondary changes in the bone as well. Let us not forget the tendency in certain families toward these bony changes. When I suspect hypertrophic changes in middle-aged patients, I

first look at the fingers and if I see a Heberden's node I am pretty sure of osteoarthritis. If I do not see Heberden's nodes, I hesitate to make a diagnosis of osteoarthritis.

About the agglutination reaction, as Dr. Boots pointed out, this is of great interest to students of arthritis not only from the theoretical but from the practical side as well. The agglutination reaction must have some significance. We cannot say it is merely an interesting phenomenon; it is more than that. It seems to me we have in a positive agglutination reaction of hemolytic streptococcus a very important lead in the diagnosis of the disease. It is present in a very high percentage of the cases, particularly if you will limit statistics to those patients who have had the disease for some little time. I will admit that in the early stages it is absent. But with a technician who is used to reading the agglutination test, a very high percentage of rheumatoid arthritis patients will give a positive reaction. Its practical value is in differential diagnosis.

DR. ERNEST E. IRONS, CHICAGO.—I suppose that by this time we would all agree that one of the characteristic features of atrophic arthritis including the ankylosing type Dr. Miller described, is infection and that one of the most characteristic factors in the hypertrophic type of osteoarthritis is the group of changes that come with advancing age. There are a number of other factors which are perhaps not quite so clearly associated with one or the other type of arthritis. I think that we ought to develop a little further the idea that was referred to briefly by Dr. Cecil, namely, the tissue peculiarities of the patient himself. This difference in tissue reaction to trauma is characteristic of races, of families, and sometimes of individuals. A surgical operation may in one person heal in a few weeks, leaving a line scar with very little redness. In another patient operated upon by the same surgeon at the same time, a marked keloid may develop. Applying this to arthritis, undoubtedly there are different degrees of resistance to infection in different people. Certainly, different families differ in the incidence of chronic atrophic arthritis. The changes of senescence appear much earlier in one patient than in another. So resistance to infection and the quality of tissue reaction in patients must, I am sure, play a large part in determining whether the patient will have arthritis, and if so, the type.

DR. EDWIN W. RYERSON, CHICAGO.—Dr. Miller has shown very well in his lantern slides the characteristic changes of the various types of arthritis. One significant point to me is the number who develop arthritis that we have missed in the past. The other point is the chronic ankylosing arthritis, of which in Chicago we have seen a number of examples. I wish to emphasize the importance of applying apparatus to the individual who is beginning to get ankylosis of the spine. If he is not treated by a Taylor brace or plaster jacket or a bivalve stirrup jacket, he is certain to become very kyphotic, and a long curve in the spine will occur. For years I have seen an old dentist walking along with his back bent to a right angle, simply because no one, when he was seen at the early stage of this disease had thought of putting on any apparatus. So we cannot emphasize too much the value of orthopedic common sense in some of these cases. It is worthy of remark that some of the painful arthritic spines can be very greatly relieved, first by traction in bed if the condition is very acute, and second, by suitable apparatus to hold them upright so as to prevent lateral and anteroposterior motion of the spine. If these measures are carried out, the patients will be greatly relieved and in the end be definitely benefited by orthopedic procedures.

DR. RUSSELL L. CECIL, NEW YORK, N. Y.—I would like to ask Dr. Ryerson how soon should braces be put on those backs. Is there danger of putting them on too soon and losing motion in the back?

DR. RYERSON.—Answering Dr. Cecil's question, if motion is the cause of great pain and if it is a spine that is going to ankylose anyway, what difference is it if you put on a brace and do obtain a painless ankylosis of the spine, but on the other hand, a rested joint is very much more likely to recover motion than if allowed to go on without a brace.

DR. LORING T. SWAIM, BOSTON, MASS.—I agree absolutely with Dr. Ryerson. I believe that early fixation of the spine prevents the process from going too far and producing the bony changes which we see in the spine. I have one patient in a jacket who was stiff;

at the end of five years he is beginning to get back some lumbar motion. Bony ankylosis has not taken place. I believe because constant trauma was prevented. All the protective muscle spasm goes with support. The tense neck and adductor spasm of the legs disappears at once with adequate support in a jacket.

DR. JACOB S. KOMINZ, ROCHESTER, N. Y.—I wonder if infection plays the same part in causing the ankylosing type of spondylitis that it does in arthritis of other joints. I ran across a couple of patients that have been under observation for several years. One was a carpenter who specialized in laying floors. Following a throat infection, though the tonsils were removed, he developed an ankylosing spondylitis which has progressed to marked degree. The other was a service man in a gasoline station who took a particular interest to see that the cars in his station for greasing were carefully done and worked in the greasing pit himself. This necessitated much stooping on his part. He developed one of the types of ankylosing spondylitis. I wonder if those who have used the back more actively and persistently than other individuals are predisposed to that type of spondylitis?

I would like to ask Dr. Miller this question. We frequently run across in doing compensation work, individuals who evidently had slight hypertrophic arthritis of the back, and suddenly when some injury draws attention to it, have a chronic back which causes a lot of trouble. Second, people are going about who have marked evidence of hypertrophic changes in the spine and yet have no symptoms whatsoever, and only incidentally when x-rays are taken for some other purpose, these marked bone changes in the spine are discovered. I would like to ask how to interpret these cases.

DR. JOSEPH L. MILLER, CHICAGO.—Regarding ankylosing spondylitis, I can easily see how infection can play a rôle. In most of these cases we have no idea as to where the infection originated. I think from my own experience in the Cook County Hospital, where we have a great many colored people, that by far the most common cause is gonorrhea. This condition may appear in the spine without any involvement of the joints of the extremities.

Now, why some patients have pain in osteoarthritis and others do not, we do not know, as the cause of the pain is unknown. Anton Fischer says very positively that it is not due to pressure on the nerve roots. It is true that in England workers who handle heavy steel get lumbago. These people may rest up for a week; then return to work; and then find that the pain recurs. Osteoarthritis, which is usually not a disabling disease, can cause disability in people following certain occupations.

Just a word about osteoarthritis of the knee. We frequently see this disease in women who have become obese after the menopause. The pathology in the knee of late cases of rheumatoid arthritis and advanced cases of osteoarthritis may be almost identical. Nichols and Richardson called attention to this point. In their work the specimens from these two types of cases were so similar that they thought the two diseases were related. If I understand rightly, these polypoid changes come from the synovia. If there is no synovia left, no polypoid changes take place.

DR. R. GARFIELD SNYDER, NEW YORK, N. Y.—The classification proposed by Dr. Boots and Dr. Miller seems, on the whole, to be the most satisfactory method outlined to date. However, they fail to emphasize the importance of the very large group of cases that can only be accurately classified as mixed arthritis. Statistics differ, of course, according to location, but it has been our experience that at least 50 per cent of the total number of patients treated belong to the mixed group. The importance of properly classifying these cases lies in the fact that the term "mixed" serves as a reminder in outlining treatment that there is an infectious, as well as a metabolic element to deal with.

Dr. Boots and Dr. Miller in their paper state that, although the majority of patients with rheumatoid arthritis are between the ages of twenty and forty, there are patients eighty years of age who have arthritis. I would like to emphasize that whereas in the patients under thirty years of age, tonsils are the most likely source of infection, in the patients between the age of forty and seventy years of age, the foci are usually chronic and not infrequently are silent in character. Sinuses, gallbladder, prostate, and genitourinary tract are the sources

most often suspected. It has been my experience, and I am sure the experience of all of us, that the efficient removal of these foci, regardless of the age of the patient, causes an excellent therapeutic result.

DR. M. HENRY DAWSON, NEW YORK, N. Y.—I should just like to say a word or so concerning a series of cases of Marie-Strümpell arthritis which we have studied in the past six years. In all we have had sixty examples and in general our statistics agree with those of Anton Fischer which Dr. Miller has quoted. Forty-eight of our cases occurred in males and twelve in females, a ratio of four to one. This curious sex distribution is, of course, quite different from that which occurs in rheumatoid arthritis. Nevertheless, I believe that the two diseases are essentially the same except for their anatomic localization. In relation to the sex distribution of the two conditions there is one interesting and important fact. Just as Marie-Strümpell or rheumatoid spondylitis is more common in the male, so also it is a "purer" disease in this sex. By this I mean that it is more strictly confined to the spine. In the female, on the other hand, there is a definite tendency for the disease to assume a "mixed" form with simultaneous involvement of both the spine and peripheral joints.

One point which we have studied very carefully is the relationship between gonococcal infection and the development of rheumatoid spondylitis. This is a widely held concept, but we have been able to obtain very little evidence to support it. One occasionally sees patients with rheumatoid spondylitis who have had gonococcal infection but to prove a relationship between the two conditions is almost impossible. Only two of our sixty patients gave a positive gonococcal complement fixation and in our experience gonococcal infection has not been any more frequent in rheumatoid spondylitis than in many other diseases. I think that this question should be examined very carefully before any conclusion is drawn.

In one very minor point I find I must disagree with Dr. Miller. He stated that the involvement of the hips and shoulders in Marie-Strümpell arthritis was frequently osteoarthritic in nature. This has not been our experience. In nearly one-fourth of our cases, there has been involvement of the hips or shoulder joints, and roentgenograms have invariably shown that the changes were rheumatoid in nature.

DR. JOSEPH L. MILLER, CHICAGO.—The only description of the hips I found was in Buckley's article where he described simply the type of picture of osteoarthritis. I found one other reference to osteoarthritis. I am very glad to hear Dr. Dawson say that the majority of his cases were really rheumatoid arthritis.

DR. M. HENRY DAWSON, NEW YORK, N. Y.—Gilbert Scott of London has shown, and it has been our experience, that 90 per cent of all cases of Marie-Strümpell spondylitis show involvement of the sacroiliac joints.

DR. PHILIP LEWIN, CHICAGO.—I think that Dr. Dawson's statement can be compared with what we see in spurs of the os calcis. The presence of gonorrhea does not prove that the spur on the os calcis is due to the gonococcus any more than Marie-Strümpell disease in the spine is due to the same organism.

DR. RALPH H. BOOTS (CLOSING).—Realizing that Lord Horder is an honored guest, it seems in poor taste to engage in controversy with him concerning my ideas of the etiology of these two types of arthritis; however, I refuse to leave you with the impression that their causes are definite in my mind. My statement in regard to osteoarthritis was "that it might be possible that it is due to the summation of joint insults during the entire time of one's life." In regard to rheumatoid arthritis, it was stated that the true etiology is not definitely known; however, in view of the presence of hemolytic streptococcus agglutinins in the blood of these patients, it suggests that the disease is connected in some way with this infection. The finding of streptococcus agglutinins in the blood of these patients seems to us the most important advance made recently in this disease. This work has been confirmed by a number of investigations and by blindfold tests by Cecil, Dawson and others.

I should be glad to know if the pathologic picture of the nodules found in fibrositis by Dr. Hench is similar to the one which I have shown in the subcutaneous nodules of rheumatoid arthritis.

DIFFERENTIAL DIAGNOSIS OF ACUTE RHEUMATIC FEVER*

R. A. Kinsella, A.M., M.D., St. Louis, Mo.

IN THE usual situation, the diagnosis of acute rheumatic fever is readily made. This disease has an individuality which no other disease can completely imitate. However, it shares with other diseases certain features, and it is in this field of common clinical display that the clinician hesitates before coming to a conclusion. It is the purpose of this communication to delineate the individuality of rheumatic fever and at the same time point out the features that are possessed in common with other forms of articular rheumatism.

One is impressed at the outset with the irregular distribution of the disease in the United States, so that the experience of a physician in the Mississippi Valley differs sharply from that of a physician in New England, where the incidence of the disease is, roughly, five to seven as great. During the past twelve years only 74 patients with acute rheumatic fever were admitted to St. Mary's Hospital in St. Louis, a general hospital of 250 beds; whereas, over half that number would be admitted to a hospital of comparable size in New York City, in a single year. At the same time, 75 per cent of the patients at St. Mary's Hospital were between the ages of five and fifteen, an age distribution fairly characteristic of the disease in the United States.

One of the first features of rheumatic fever that contributes to the individuality of the disease, therefore, is the early stage at which the disease occurs This age factor is emphasized in another way. Of forty-four patients coming to necropsy, either showing definite anatomical stenosis of the mitral valve or having a history of recent rheumatic fever, seven showed lesions in the heart muscle which might be regarded as specific, and in this "specific" group the average age was twelve. That the remainder of this group of forty-four could have acquired an average age of fifty-two further emphasizes the diminished virulence of the disease in the Mississippi Valley, or indicates a lower incidence of subsequent intercurrent infections. Of course these statistics are dependent on the criteria employed for diagnosing the cardiac lesion as specific of rheumatic fever.

This leads us to the discussion of the specificity of the cardiac lesion. It can be shown that there is a lesion not imitated closely by streptococcal infections or any other bacterial infection with which we are at present familiar.

The constancy of the cardiac lesion is remarkable. It may be safely asserted that no patient acquiring rheumatic fever, before the age of twenty, can escape some clinically discoverable cardiac involvement. Among the 74 patients having a clinical picture of acute rheumatic fever, none was free from definite cardiac valvular disease, although two patients acquiring the disease after the age of twenty-five, showed little of the disease in the heart, five years later.

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The age incidence and the constancy of cardiac involvement are the chief factors contributing to the individuality of rheumatic fever. The clinical features are indeed striking in the average case. The migratory character of the articular signs is always emphasized, but this feature is probably not as important as the transitory quality. By migratory we mean the peculiarly irregular visitations which the disease makes to any joint or joints in the body at a given moment. By transitory we refer to the fact that each visitation lasts only a limited number of days—usually three to five—although a remnant of stiffness and soreness may persist for several weeks. It is extremely important to remember that acute rheumatic fever discards its arthritic phases, and only the cardiac involvement is permanent. The persistent movement of the heart may be responsible for a different type of healing, or a more extensive lesion; and subsequent infections, often streptococcal in nature, may contribute to further damage of the heart, but do not ever further affect the life of the joints.

Unfortunately, the definite individuality of acute rheumatic fever is not always developed within a period of a few days during which the physician desires to make a diagnosis.

It becomes necessary, therefore, to consider other inflammations of joints which may display similar clinical patterns.

1. The first of these is Still's disease. This remarkable disease makes its appearance in childhood, usually before the age of ten. Its beginnings are usually not abrupt, as in the average case of rheumatic fever. There is an early preference for small joints, and a given joint, once affected, seems to resist the healing process and rather to become more and more disabled by painful and tender swelling. The articular involvement migrates always with emphasis on the small joints, and shows little tendency to abate. Finally, deformity and devastating disability prevail. The spleen and lymph nodes are often enlarged and subcutaneous nodules are more frequent than in acute rheumatic fever. Finally there is no characteristic cardiac disturbance in Still's disease.

2. Acute rheumatoid arthritis may present a situation in which differentiation from acute rheumatic fever must be deferred for weeks, until sufficient evidence has accumulated to make diagnosis certain. These comparatively rare cases are those that occur between the ages of eighteen and twenty-five, usually in female patients, in whom, red, tender swellings appear about the wrists and small joints, but also about the elbows and shoulders; and in whom the episode about each joint tends to terminate in a period of from three to five days. At this stage there is fever which seldom exceeds 101° F. The study of immunity responses is not yet defined to the point of being useful in the hands of the average laboratory technician. Another feature which greatly emphasizes the diagnostic dilemma arises from the possibility of a remission or even recovery. The diagnosis of acute rheumatoid arthritis is suggested by the greater involvement of small joints which may display pale globular swellings; and the complete escape from cardiac damage. But we cannot leave this discussion without admitting the possibility that some cases of acute rheumatic fever in young adults may be prolonged, without cardiac damage; and that some cases of acute rheumatoid arthritis may recover com-

pletely; or that there may be another disease, simulating both rheumatic fever and rheumatoid arthritis which has yet to be identified. It is not my opinion that the treatment with salicylates offers a differential method of diagnosis. Such cases as described above are rare in this country, at least, and practically every case of rheumatoid arthritis, no matter how acute in its beginnings, always leaves permanent or progressive or recurring articular damage, whereas acute rheumatic fever always discards its articular features eventually.

3. Acute bacterial infections about joints with their available local cultures may simulate rheumatic fever in a limited way.

a. During severe infections of the mastoid with hemolytic streptococcus, there may be periarticular redness and swelling and tenderness which, in general appearance and distribution imitate the features of rheumatic fever. More frequently, of course, such localizations contain hemolytic streptococci, develop purulent centers with extending edematous surroundings, and constitute part of a fatal infection, but in no case is there any characteristic involvement of the heart. Pneumococcal infections seldom show as marked a capacity for articular distribution as that shown by hemolytic streptococcal infections.

b. The early stages of gonorrheal rheumatism may show polyarticular distribution but soon the infection settles in one joint where the fluid obtained by aspiration, while not as yellow as that obtained from streptococcal infections, is much more turbid or yellow than that obtained from joint cavities in rheumatic fever and usually contains gonococci. The percentage of polymorphonuclear leucocytes may be the same, but the quantity of pus is much less in rheumatic fever. The association with an infection in the genitourinary tract and the freedom from cardiac disease, except in the very rare instances of fulminating gonococcal endocarditis, complete the evidence in gonococcal arthritis.

c. People of middle age and beyond, usually with the structural changes of osteoarthritis, may present themselves with multiple periarticular inflammations which are acute. These inflammations are frequently characterized by edema, by positive cultures locally obtained, and by the presence of some active infective process (most often in the genitourinary tract—in my experience). There is no cardiac involvement. Recovery may occur or the disease may become chronic and strikingly imitative of chronic rheumatoid arthritis.

4. Gout: This disease usually appears at a later time in life and while sometimes polyarticular, is usually intensified in one joint, where the manifestations are out of proportion with the mild constitutional effects. The cardiac involvement in gout follows only after very many attacks and is like the involvement in vascular disease. Colchicum will not benefit acute rheumatic fever, but is often of great help to the sufferer from gout.

DISCUSSION

DR. T. DUCKETT JONES, BOSTON, MASS.—To further discuss before this Society the differential diagnosis of rheumatic fever from that of the various forms of arthritis would seem like "carrying coals to Newcastle." There are, however, several features of the two diseases that I might mention.

Because the age groups of the majority of rheumatic fever subjects coincide with that of so-called Still's disease, these two perhaps offer the greatest difficulty as to differential

diagnosis. There can be no question but that the typical cases of each disease need not be confused, but also we must be cognizant of the fact that the two occur simultaneously. While the latter is not common, it is not unusual to see a child with definite heart disease of the rheumatic fever type and active carditis in progress, who also shows definite and progressive joint change, characteristic of Still's disease. There are, however, two types of Still's disease which offer difficulty. Occasionally one sees children with fever, and severe joint pain, swelling, etc., no evident heart disease, and the patient recovers and is seemingly well. After varying periods of time there may be recurrences of this same episode, and the process continues with this story for several years prior to the development of permanent or appreciable joint change. I know of no diagnostic methods which are proof positive of either rheumatic fever or Still's disease in this group, and the diagnosis must rest on the ultimate course of the disease process. A further type of Still's disease offering difficulty in diagnosis is the rare patient with pericarditis early in the course of acute illness. In some such cases evident slight enlargement or hypertrophy of the heart has been observed for a period of several years without evidence of valvular disease, and the subsequent course does not seem to be similar to patients with heart disease as a result of rheumatic fever.

In postadolescents and young adults the difficulty of differentiating between rheumatoid arthritis and rheumatic fever may be impossible. Typical cases of either may be easily differentiated as Dr. Kinsella has noted. Here again the two diseases may occur simultaneously. Transient changes demonstrated by electrocardiogram may show the presence of an active heart lesion while examination of the joints may show progressive, permanent joint damage. Cases of acute polyarthritis in this age group often may be indistinguishable from rheumatic fever and the diagnosis definitely determined only after a long period of observation. Salicylate therapy has not seemed to us to have been of great diagnostic aid.

Of considerable importance in connection with such a discussion of differential diagnosis is whether or not rheumatoid arthritis and rheumatic fever are in any way etiologically connected. This has been a subject for discussion for many years, and I see no way in which it may be settled at the present time. While the characteristic life story of the two diseases varies, one showing heart damage and the other progressive joint damage, there are points of similarity which make one wonder if they may not be to some degree related. However, we have not seen any appreciable instances of rheumatoid arthritis develop in a large group of rheumatic fever subjects followed for a number of years. The suggestion that the variation between the two diseases is dependent upon age, that there are strong similarities between the histologic picture of the nodules noted in the two, that both have chronic and recurring courses, as well as the fact that there are certain bacteriologic and immunologic factors which seem to play a part in each, leaves the question of a close etiologic connection well muddled. I personally feel that cases in which there is a suggestion of both diseases should be carefully studied and followed, and that we will settle this possible relationship only when the agent of one or the other disease is known, and it will be possible to have specific tests.

I would also like to make a plea that this Society maintain its interest in rheumatic fever. In recent years, rheumatic fever has been shown to be a disease with pathologic changes throughout the body, and while death is usually the result of damage to the heart, there are many other important general factors, and it would be unwise to investigate the disease purely from a cardiologic point of view. Perhaps if we keep open minds and observe a large number of patients with rheumatoid arthritis and rheumatic fever, we may be able ultimately to solve many of the problems concerning the two separately, and the question of a common etiologic factor.

DR. RALPH H. BOOTS, NEW YORK, N. Y.—I am glad that Dr. Kinsella introduced a group of cases about which little has been said. These cases are occasionally referred to as "focal infection arthritis," not uncommon in older people, sometimes suspected of being due to infected prostates. This seems to be an entity quite distinct from rheumatoid arthritis.

Regarding the frequency of rheumatoid arthritis in older people, although most patients are affected before forty years of age, we must realize that many of these continue with the disease the remainder of their lives, which accounts for its frequency in older people. The patient referred to by Dr. Snyder was a woman, so the prostate was not a factor.

DIFFERENTIAL DIAGNOSIS OF TRAUMATIC ARTHRITIS*

WILLIS C. CAMPBELL, M.D., MEMPHIS, TENN.

TRAUMATIC arthritis constitutes the largest class of joint affections, yet comparatively little interest seems to have been manifested. In attempting to review our records, the number was so large that a complete analysis was impracticable. In consequence, I have restricted the discussion chiefly to the knee joint, excluding such well-known clinical entities as acute synovitis, derangements of cartilages and common types of loose bodies and joint fractures. In fact, I have previously defined the type of joint under discussion as "low-grade traumatic arthritis." The etiology is mild or severe trauma causing organic changes of more or less degree within the articular structures, or repeated trauma, as may occur in certain occupations where there has been excessive wear and tear of a part by overuse, or function with faulty posture or attitudes, so that intraarticular pressure is unevenly distributed.

Arthritis associated with trauma may be divided into three groups: 1. Traumatic arthritis, uncomplicated, with evolutionary pathologic changes entirely the result of trauma.

2. Arthritis of various clinical entities in which trauma was possibly a definite instigating agent without further manifestations, as pyogenic infection, gout, etc.

3. Traumatic arthritis, in which trauma is a definite factor in exaggerating or producing symptoms but is associated with other pathologic entities, as low-grade infectious arthritis, gout, hypertrophic type of arthritis or osteoarthritis, syphilis, etc.

I. The evolutionary pathologic changes after trauma depend on the intensity of the trauma and the reaction of the individual. This reaction is well known and is simply that of an irritating process within the joint and may involve the synovia, capsule, and articular cartilages. A marked increase of synovial fluid may occur, but is by no means common. This may be followed by the formation of fibrin with more or less organization into fibrous tissue with adhesions. The villi increase in size and also in number. Beneath the synovia there may be more or less fibrous tissue reaction which may to some extent impair circulation, giving the synovia a more or less dusky hue when the joint is opened. As embryonic rests of cartilage cells are present within the synovia and the capsule, cartilaginous masses may be formed. These may be extruded into the joint as loose bodies, osteochondromatosis or synovial osteochondromatoma. The joint capsule also may increase slightly in dimension. The articular cartilage may undergo softening and liquefaction, the so-called fibrillation. Trauma to any area of articular cartilage may cause gradual disinte-

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gration as there is scant spontaneous repair in cartilage tissue. As there are no sensory nerves clinical manifestations of pain may be delayed. When such an irregular area occurs on any articular surface, further damage to the opposing articular cartilage and other structures may be brought about; thus, a progressive vicious cycle is established. Beneath the cartilage the cavernous extremities of the bones undergo osteoporosis which must be distinguished from atrophy of disuse. Irregularities within the joint may induce hypertrophic changes, as the formation of osteophytes about the margins of the articular surfaces. In other words, from constant irritation of a more or less incongruous joint a typical localized osteoarthritis may be produced. In a large majority of cases only slight organic changes in the joint occur with a restoration to normal within a short period of time, but all of these changes are possible. Loose bodies in osteochondritis dissecans (probably due to trauma), various derangements of cartilages and gross fractures are complications and etiologic factors in traumatic arthritis but are definite clinical entities, and as stated above are not included in this discussion. Osteoporosis is a physiologic process which follows every toxic or traumatic irritation, and possibly is caused by some vasomotor influence through the sympathetic system, which induces an active increase of circulation to the part. It is manifested by the absorption of lime salts, and is demonstrated in the roentgenogram by a characteristic mottling of the cavernous extremities. Atrophy of disuse is a gradual encroachment of the marrow on the cortex with diminution in size of the entire bone and usually of much longer duration.

These pathologic changes attributable to trauma may resemble closely those of other pathologic processes, but there is often some factor by which differentiation can be made, such as the characteristics of granulations in tuberculosis, and the more intensive round cell infiltration of an infection.

The symptoms of pure traumatic arthritis of the knee are pain usually with slight swelling. Occasionally an effusion may be present, but often there may be the appearance of a perfectly normal knee. On motion crepitation is present which is due to thickening of the capsule and synovial villi; friction fremitus, as in pleurisy, may be elicited occasionally. The surface heat is not increased as a rule, which is a differential factor from an infectious process. Motion is not limited usually though muscle power of the quadriceps may be decreased markedly. Pain may be elicited in extreme flexion and extension. Differentiation from other low-grade affections cannot always be made except by a definite history of trauma followed immediately by physical signs and symptoms, and the absence of other factors, as fever. The roentgenogram in the early stage may demonstrate osteoporosis adjacent to the joint but often there is no abnormality. Only in those under thirty years of age can one be fairly certain that a process is entirely traumatic.

II. In arthritis of various types trauma may be the instigating factor; for example, after a definite mild injury to a knee, a pyogenic affection may occur which causes characteristic pathologic changes. The same is true in neoplasms and tuberculosis. In gout a slight trauma frequently causes acute arthritis as indicated by sudden effusion of the joint, and it is usually quite difficult to convince the patient that such a violent reaction could not occur

without some deficiency in the quality of his own organism. The appearance of such a patient usually is suggestive and as a rule the age is above forty years. The blood uric acid is increased. A purin-free diet and colchisal usually give rapid relief. Although the process is instigated by trauma, the important fact in this type is not traumatized tissue, but the active clinical entity requiring differential diagnosis and treatment, which usually occurs with no history of trauma.

Traumatic arthritis is usually confined to one joint, though it is occasionally bilateral. I have seen evidence of trauma as an exciting agent of progressive polyarticular arthritis. This was probably brought about by the increased susceptibility of traumatized tissue to infection, followed by a selective invasion of other joints.

III. Traumatic arthritis in which trauma is a definite factor but associated with other definite clinical and pathologic entities, forms by far the largest and most important group in which trauma plays a practical rôle. In such cases the patient usually is approaching middle age or above, though age is not always a question of years.

Osteoarthritis or the hypertrophic type of arthritis, more frequently is the complicating agent. For instance, an obese lady of fifty years has a fall in the street and definitely bruises and injures the skin and soft structures, she is taken home and given a few days' rest in bed, then she limps about for a few weeks before she consults the doctor. Definite tenderness with or without swelling may be elicited. The roentgenogram shows extensive hypertrophic changes in both knee joints, often more severe in the opposite knee in which there are no symptoms. Often a history of back pain, or some previous symptoms in other joints, may be elicited. A roentgenogram of the spine may demonstrate extensive hypertrophic changes. Trauma may often induce persistent symptoms when osteoarthritis is present in the spine. The question frequently arises as a medicolegal equation; how much of the disability may be attributed to trauma? how much to the previously existing disease?

In gout, syphilis, and low-grade infectious arthritis, there may exist the same relation of trauma, in which there can be no doubt that trauma of sufficient severity to play a definite part had occurred. Even in gross fractures and injuries into joints, or when there has been a long period of fixation of an adjacent normal joint, definite arthritic changes from other causes may be by far the most disabling factor.

Frequently the complications secondary to traumatic arthritis are far more disabling than the original injury. Osteoporosis is apparently a normal physiologic vasomotor response to trauma as evidenced by the absorption of the lime salts from the ends of fragments following a fracture. After a traumatic injury to a joint, this process may become excessive and manifest itself in the soft tissues by swelling, pain, hyperemia, and cyanosis. Roentgenograms reveal a mottling of the bone with marked decrease in density which extends for a considerable distance from the joint involved. Osteoporosis to a pathologic degree is rare in an individual under forty years of age.

Uncomplicated traumatic arthritis exists only as a definite clinical entity in the young. Such cases are observed most frequently in young male athletes, and the pathology has been described above. Ample opportunity has been afforded to explore such joints when symptoms persist, and the pathology is quite definite as described above.

When there is definite trauma associated with symptoms suggesting some other affection, as osteoarthritis, syphilis, low-grade infectious arthritis, or gout or tuberculosis, as careful a differential diagnosis is required as if the physical signs and symptoms had occurred without trauma, and often a biopsy is essential though not of itself always conclusive. In fact, in all traumatic lesions of joints the possibility of a coexistent affection must always be duly regarded, and the arbitrary diagnosis of traumatic arthritis should be made only with the greatest care and differentiation.

DISCUSSION

DR. CHARLES L. LOWMAN, Los Angeles, Calif.—I greatly appreciate Dr. Campbell's paper. He has emphasized considerations of a wide scope. Of especial interest to all orthopedic and industrial surgeons is his comment on (a) the compensation insurance and medicolegal aspects; (b) the exacerbation of existing, perhaps quiescent arthritic process by intercurrent surgery; (c) the recognition of osteoporosis following traumatic lesions; (d) the diagnostic difficulties in relation to age.

We think of traumatic arthritis as local or remote, with reactive changes in immediate region of injury, in or near a joint, or in one or more adjacent or remote joints to which the jar or stress has been transmitted at the time of injury. (For instance, changes may occur in the spine when the major trauma is in the legs or pelvis, or may be in the shoulder, due to a fall on the hand injuring the wrist area.) Traumatic arthritis is characterized by capsular thickening, irritation of synovial fringes, contusions, cracks or compression reaction in articular cartilages, interference with function, pain, tenderness, muscle atrophy, swelling, and often crepitation. X-rays often show cartilage changes, spurring or lipping, increased density of joint margins at the area of injury with adjacent atrophy not shown on the opposite side. At later stages, an osteoporosis below the lesion may also be shown, which may be just adjacent to the joint or may involve a more extensive area; for instance, the whole wrist and hand when the lesion is in the elbow or shoulder, or the whole foot after leg fracture or sprained ankle.

In a young person, definite relation to specific trauma without presence of arthritis in other localities, is a great help in diagnosis. Yet, the coexistence of arthritis in other locations is no criterion of the nonexistence of a real traumatic arthritis. In compensation cases, especially where the patient is beyond the age of forty years, the degree of static stress with incident moderate chronic arthritis, or the presence of definite rheumatoid or osteoarthritic changes, makes it difficult to judge the worker's status and compensability. But I feel that we are justified in giving the benefit of doubt to the worker if he has been continuously employed, and has given continuous service until interrupted by the injury. He has a right to expect a protection from time loss, and it seems as though his employer should bear the burden of proof, if he was not wise enough to ascertain whether or not the man had an arthritis before he hired him.

Dr. Campbell correctly points out that osteoporosis is probably due to a sympathetic nerve upset, which may occur especially in the presence of constitutional tendencies, such as glandular imbalance. Its occurrence with traumatic arthritis greatly prolongs the convalescence, giving a sensitive painful member which may be made worse by careless or improper handling. One must not be confused as to acuity of symptoms when the patient may have had faulty physiotherapeutic treatment, such as the improper use of heat, either too deep or too prolonged. Pain and spasm are reduced by heat, and the patient feels a

sense of relief, but many use the faulty technic of following it with active movement. The heat congests the area involved, enlarging the fringes. Unless they are drained and lessened in size by elevation and by depleting massage, movement will pinch and irritate the joint constituents enough to produce more swelling and tenderness, resulting in continuing spasm. Thus the ignorant may produce the very condition that they are trying to remedy.

We should not only make a diagnosis of the specific lesion but we should also continue to diagnose the status at various intervals. When a technician reports that limitation of motion at a given point has not changed for two weeks, new x-rays should be taken, diagnosis of the new status made, and treatment altered.

If we keep in mind the picture Dr. Campbell has so clearly shown us of what is occurring in the traumatized joint, we will not be likely to go wrong in treatment, and much time and cost will be saved for all concerned.

DIFFERENTIAL DIAGNOSIS OF TUBERCULOSIS ARTHRITIS*

FRANK D. DICKSON, M.D., KANSAS CITY, MO.

IT IS extremely interesting to find a condition of as great antiquity as tuberculosis still being actively discussed today. That such an old problem is still an active one indicates that we have not yet completely solved it, else the need for discussion would be gone. Yet it is generally believed today that we have the means at our disposal of curing tuberculosis if the diagnosis is made early and proper treatment at once instituted. It would seem then that our problem must be mainly one of early diagnosis; unquestionably this is so in tuberculosis of the joints.

The diagnosis of tuberculous arthritis after years of study and countless observations still presents many difficulties, at least in the early stage of the disease. This is a fact of some economic and sociologic importance since tuberculous arthritis, while not the cause of such widespread disability as chronic arthritis of other types, does play no small part in the production of the physically handicapped; it has been estimated that tuberculous joint disease is responsible for approximately 20 per cent of all the cripples in this country. Moreover while chronic arthritic diseases exhibit but little tendency to shorten life, the mortality from tuberculous arthritis, so far as can be determined, is approximately 20 per cent. From the point of view then, both of prevention of crippling and disability and as a life-saving measure, the diagnosis of tuberculous arthritis, particularly in its incipiency, is worthy of more general study and better understanding by the profession than it has had up to the present time.

Tuberculous arthritis for the purpose of this discussion may be separated into three groups: (1) Monarticular arthritis; (2) multiarticular arthritis; and (3) polyarthritis or "tuberculous rheumatism." Of these three groups the monarticular form is by far the most usual and represents the commonly accepted understanding of tuberculous arthritis. Involvement of several joints in the same individual by a tuberculous process does occur, but such multiarticular involvement is not frequent. Tuberculous polyarthritis or tuberculous rheumatism has not been generally accepted as an entity, but since there is no incontrovertible proof that it does not exist, we are compelled to accept it at the present time as a possible form of tuberculous arthritis.

Monarticular Tuberculous Arthritis.—The diagnostic criteria of monarticular tuberculous arthritis vary to some extent with the stage of involvement of the joint under investigation, and any attempt to propose a diagnostic plan must take this fact into consideration. Broadly speaking, we should look upon tuberculous arthritis as having two stages in its course: an early stage when the disease is without radiologically visible osseous foci and therefore

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synovial or pseudosynovial; and a late stage, when bone involvement gives a more or less definite picture radiologically. It is in the early stage of the disease that diagnosis is of paramount importance since it is at this time, if ever, that cure with function is possible; in the later stages, irreparable damage has been done and complete eradication of the involved joint becomes imperative if the local disease is to be arrested and perhaps life preserved. By the early stage of involvement is meant that period in which, as stated, the disease has attacked only or largely the synovia, and there has been no involvement of bone, or at least involvement to such a slight extent that it cannot be detected by x-ray. Such important and often difficult early diagnosis may be arrived at through information derived from investigation along several lines; these may be catalogued as follows:

1. History
   - Family and past medical
   - Age
   - Present condition
   - Trauma
2. Site of involvement.
3. Constitutional symptoms.
4. Local objective findings.
5. Laboratory examinations.
6. X-ray findings.

History.—For years the careful investigation of the history of a suspected case of tuberculous arthritis has played an important part in diagnosis and such information is just as necessary today as in the past.

A careful inquiry into the family and past medical history may yield entirely negative results but may disclose contact or possibility of contact with infection, some previous manifestation of tuberculosis, visceral or glandular, or loss of health and vigor, all important leads.

Age is important as monarticular tuberculous arthritis is most common under the age of fourteen. Infection does, however, occur in adults and even in late life, and the possibility of such late occurrence should be borne in mind constantly in investigating any case of monarticular arthritis. We have had in our clinic a number of cases of adult joint tuberculosis and several cases of patients between the ages of fifty and sixty-five years.

The character of the onset and course of the joint involvement is perhaps the most important part of the history. The onset is characteristically insidious; stiffness and interference with joint movement, slight swelling, and little or no pain is usually complained of or noticed by the parents for some time before pain and increased swelling suggest that the condition is serious. The late appearance of pain and tenderness is a most important point in differential diagnosis between tuberculous arthritis and other forms of arthritis, since in the latter pain is usually an early and important symptom. The course of the disease is indolent and characterized by remissions and exacerbations; the general trend, however, is progressive in character. The periods of remission are very deceptive and are frequently responsible for failure to make an early diagnosis.

Th history of a recent injury, six to twelve weeks previously, with a normal joint during the interval is suggestive as the part played by trauma as a predisposing cause in tuberculous arthritis has been definitely established.

Site of Involvement.—The joint involved will give some help in diagnosis, since certain joints are the favored site of tuberculous infection. While it may be true that these same joints, by reason of their exposure to trauma, are likewise the most frequently attacked by other forms of infection, this fact does not lessen the importance of established statistics on joint involvement in tuberculosis. In 158 cases of tuberculous arthritis the following joint distribution was found: Spine 62; hip 41; knee 25; ankle 11; wrist 10; sacroiliac 6; shoulder 2; elbow 1. This distribution conforms fairly closely to that of other observers.

Constitutional Symptoms.—Constitutional symptoms are frequently absent or must be diligently searched for. There may be some sign of toxemia if the primary visceral or glandular infection is extreme or active. Loss of weight and poor health may occur early but may be late manifestations; when present they are suggestive but like toxemia are found in other forms of arthritis. High temperature is not characteristic, in fact little temperature reaction occurs in most cases; a normal or subnormal morning temperature with an elevation to 99° in the late afternoon or evening is perhaps the most common temperature finding. A careful examination of the throat, nose, and ears should always be included in the general investigation, since the presence of a frank throat or nasal infection is suggestive of a toxic arthritis rather than tuberculosis.

Local Objective Findings.—The local clinical findings play a very important rôle in diagnosis; they are still our main reliance.

Limitation of joint movement and a slightly swollen and moderately painful joint should arouse a suspicion of tuberculosis, particularly in children. The character of the swelling is helpful as it is a boggy, doughy enlargement due to swelling of the synovia, not the fluctuating swelling caused by excess fluid in the joint. Another suggestive local finding is muscle atrophy often out of proportion to the history of the duration of the condition; this early and extreme muscle atrophy is probably best explained by the fact that interference with joint movement has been present for some time before inflammatory symptoms become severe enough to attract attention. Calvé and Ombredonne emphasize swelling of the adjacent lymph glands as a diagnostic point but such swelling is found in almost every joint infection and does not seem to rank as important in differential diagnosis.

Laboratory Examination.—The blood count in our experience and that of many observers has not proved helpful in the early diagnosis of the disease; however, a moderate degree of anemia is often present. Von Pirquet and Mantoux tests should always be made; if positive they afford little information, if negative they assure us that the patient is free of tuberculosis and, therefore, in the suspected joint. A Wassermann test is necessary for differential diagnosis, since a chronic syphilitic synovitis with its painless effusion may simulate a tuberculous process. Guinea pig inoculation with material aspirated from the joint gives important information in a high percentage of

cases. Guinea pig inoculation should be made subcutaneously and two guinea pigs used. Unfortunately, in early cases the material secured by aspiration is not pus but a clear amber fluid, often bacteriologically negative, and false negatives often result; however, a fairly high percentage of positives has been secured by guinea pig inoculation, as high as 72 per cent in proved cases. Histological examination of material obtained at biopsy is of course very informative but even here a false negative is possible if the material obtained is inflamed but not infected with tubercle bacilli, for there is no characteristic histology unless a true tuberculous reaction has been set up. Histologic diagnosis, however, is positive in about 94 per cent of early cases. It should be stated, however, that at the present time there is a very generally held opinion that diagnostic arthrotomy in early cases is a somewhat hazardous procedure because of the danger of establishing draining sinuses; many are of the opinion that it should not be used in early cases but only in advanced or moderately advanced cases as a preliminary to excision. On the whole, it may be said that while laboratory examinations are helpful in diagnosis they are by no means conclusive and that of these laboratory tests guinea pig inoculation is probably the most useful in early diagnosis.

X-Ray Findings.—X-ray examination is usually negative before bone involvement occurs; certainly negative x-ray findings in the early cases do not exclude tuberculosis. One finding is suggestive if present; namely, decalcification of the ends of the bones entering into the formation of the joint; such a decalcification is probably a disuse atrophy and not an evidence of bone involvement.

Finally, there is one diagnostic test which cannot be placed under any of the headings outlined: This test is sometimes called Thomas' test. In carrying out this test a provisional diagnosis of tuberculous arthritis is made and the involved joint is put at complete rest in a cast. If the symptoms rapidly disappear; i.e., have gone in six weeks, the cast is removed and use of the joint permitted without weight bearing. If under such guarded activity no signs of recurrence appear increased liberty is allowed under strict supervision. A child who has a transient attack of arthritis from pharynx or intestine soon sets himself free and returns to activity; on the other hand, return of warmth, swelling and limitation of joint movement indicates a tuberculous involvement and rigid treatment.

It should be clearly understood that what has been said up to this point refers to early diagnosis. In the late stages with bone involvement and destruction, diagnosis should present little difficulty. The history of long-continued joint symptoms with periods of remission and exacerbation, the characteristic boggy swollen joint without evidence of acute inflammation, the muscle atrophy and joint deformity, and finally x-ray evidence which at this time is positive should readily establish the diagnosis. X-ray evidence in this stage is most important and one or more of the following features of bone involvement will be found:

1. Uniform thinning of the cortex of the bone.
2. Destruction or thinning of the articular cartilages.
3. Decalcification of the bone ends.

4. Lack of new bone formation.

5. Presence of a focus of bone destruction (usually in the epiphysis).

6. Failure of the process to extend along the shaft but a tendency to involve the neighboring joint.

In this stage biopsy is not only permissible but desirable and should always be carried out.

Multiple Tuberculous Arthritis.—The diagnosis of a multiple tuberculous arthritis should not be difficult and a discussion of it need not detain us long. The involvement of one or more joints in the same individual by a tuberculous infection occurs but not frequently. In our series of 158 cases it has occurred but 6 times, or 3+ per cent; in Ghormley's series of 135 cases (J. Bone & Joint Surg. October, 1926) it occurred 4 times or 3 per cent. However, in a series of 168 cases of Brav and Ghormley, it occurred in 13.1 per cent (J. Bone & Joint Surg. October, 1934). In our series the distribution was as follows: Two separate spinal foci 1; spine and knee 2; spine and both hips 1; knee and wrist 1; hip and wrist 1. The diagnosis seems quite clear when, with an existing tuberculous joint infection, a second or third joint becomes involved with characteristic local signs and supporting laboratory findings. As additional suggestive evidence we have the fact that the joint involvement is not symmetrical as it so frequently is in arthritis due to other causes, nor do the several joints become active at the same time but successively with a definite interval of time between each new involvement; at least simultaneous involvement of several joints has occurred but once in our experience in a child in which a tuberculous infection in a knee and wrist became active at about the same time. It is generally thought that the involvement of more than three joints indicates that the arthritis is probably not tuberculous.

Tuberculous Polyarthritis (Tuberculous Rheumatism).—While a number of observers beginning with Bonnet in 1845 have suggested the tubercle bacillus as a possible cause of polyarthritis it was Poncet in 1897 who definitely called attention to the relation between tuberculosis and rheumatism and described the so-called "tuberculous rheumatism." Poncet described two forms of tuberculous polyarthritis: (1) the acute or subacute form, a polyarthritis resembling acute rheumatism; (2) the chronic form resembling the atrophic and hypertrophic polyarthritis. Poncet based his diagnosis on a tuberculous family history, the presence of acute or quiescent tuberculous foci, visceral or glandular, or the presence of an established tuberculous joint lesion preceding, coincident with or following a polyarthritis. Studies were made of this condition during the next twenty years mostly by French workers but without results which attracted much attention. In 1920 Leonard Findlay reported *(Glasgow Medical Journal)* three cases of tuberculous rheumatism in children, one of which was proved at autopsy; all were associated with active visceral or glandular tuberculosis and all resembled very closely in symptomatology acute articular rheumatism. In 1928 Loewenstein and Reitter, using a special cultural method, published reports in which they claimed as high as 70 per cent of positive results for tubercle bacilli in the blood and synovial fluid of rheumatic arthritic patients. Others attempting to confirm these results were unable to do so; Kallos (Ztschr. d. Tuberk., 1932), who compiled the reports of a number of observers, states that not a single positive result by Loewenstein's method was

obtained from rheumatic arthritis, pleurisy, infectious arthritis, skin and other extrapulmonary tuberculosis. Recently the investigation of tuberculous polyarthritis has been more actively taken up in Europe, especially by the Germans, and the study of this condition has been given new impetus. At the present time the consensus of opinion seems to regard the question of tuberculous polyarthritis as still open. Those who refuse to accept it as an entity base their position on the failure to find characteristic histologic changes in repeated examinations of tissue from the joints of cases of chronic polyarthritis and the consistently negative results obtained in these cases from guinea pig inoculation. Its proponents consider it to be a polyarthritis clinically indistinguishable from other forms of this disease but caused by tuberculosis somewhere in the body, the joint manifestation being due to toxins or organisms too attenuated to produce a typical reaction but capable of producing a nonspecific reaction. They do not consider that the presence in the joints of viable tubercle bacilli is necessary for its production.

Our experience with tuberculous polyarthritis has been so limited that any attempt to speak with authority would be presumptuous; practically all our information has been gained from the work of others, therefore it is familiar to you. Personal experience and such information as has been obtainable has led to the belief, however, that tuberculous polyarthritis or tuberculous rheumatism is extremely rare. While it is possible that a tuberculous infection, especially the surgical form, may manifest itself as a rheumatism, certainly Poncet's tuberculous rheumatism is seldom seen in its typical form or at least it is seldom recognized. In an experience extending over a number of years but one case has been observed in which there was a polyarthritis of definitely established tuberculous origin, admittedly other cases may have been overlooked through ignorance or insufficient investigation. Briefly, the history of this case was as follows: A boy twelve years old presented himself with flexion contractures of both hips and marked limitation of movement in all directions. Both knees were swollen and showed slight flexion deformity. Aside from the involvement of these joints the findings were negative and a diagnosis of polyarthritis of Still's type was made. As the joints were not painful and showed no signs of activity, correction of the flexion deformity of the hips was advised and carried out. Material secured from the hip joints was examined and showed the characteristic picture of a tuberculous process. The recovery was uncomplicated but the boy soon after disappeared from observation. He was seen two years later in another clinic where he was being treated for polyarthritis of nontuberculous origin. At the time of the second examination both wrists, both knees, elbows, and several finger joints were involved. Unfortunately, before further investigation could be carried out the family again disappeared and have not been contacted since that time. This report is a very incomplete and unsatisfactory case history, but a positive histologic diagnosis of tuberculosis was made on material from two joints and subsequently many other joints became involved, and it seems permissible to consider that this case falls in the category of polyarthritis of tuberculous origin. A search of the literature has left the impression that the findings in

most of the cases of tuberculous polyarthritis reported have been similarly inconclusive and that in very few has absolute proof of a tuberculous origin of the condition been forthcoming.

In attempting to set up a picture of tuberculous polyarthritis for diagnostic purposes definite details which differentiate it from other forms of polyarthritis are difficult to fill in. Among the clinical findings in tuberculous polyarthritis which may serve as points in differential diagnosis, the following have been emphasized: absence or rarity of cardiac involvement; fewer joints are attacked than in most types of polyarthritis and one is chiefly involved; higher range of temperature than in other forms of polyarthritis; and finally, that the condition is refractory to salicylates; the latter point is especially emphasized by German observers. Kubirschky has set up six points necessary to establish the diagnosis of Poncet's rheumatism. They are:

1. The condition is refractory to salicylates.
2. Absence of endocarditis.
3. Presence of other tuberculous disease.
4. Positive tuberculin test.
5. Positive animal inoculations from synovial fluid.
6. Predominance of mononuclear cells in the synovial fluid.

Most of the reported cases fail to fulfill all these requirements.

So far then as the diagnosis of tuberculous polyarthritis is concerned it must be admitted that there seems to be no good reason that can be advanced against a tuberculous infection, producing in one of several ways a polyarthritis just as the streptococcus, staphylococcus, gonococcus, and other organisms may produce a polyarthritis. On the other hand, it must be allowed that no definite clinical picture of the syndrome of tuberculous rheumatism has been established nor has consistent experimental and laboratory evidence been produced to support the clinical evidence offered. The future may afford diagnostic tests which will show that tuberculous rheumatism and tuberculous polyarthritis do occur much more commonly than is admitted at the present time but until such methods are developed or more enlightening conclusions can be drawn from our present methods of investigation the six points of Kubirschky seem to be the most reliable criteria we have for establishing a diagnosis of tuberculous polyarthritis.

In closing, three points perhaps should be emphasized:

1. Early diagnosis is of great importance in monarticular tuberculous arthritis; such diagnosis must still be made largely on history and local evidence supported by intelligently interpreted laboratory findings.

2. X-ray is of little value in the diagnosis of early tuberculous joint involvement but is most important in the later stages.

3. The existence of tuberculous polyarthritis as an entity is still disputed, and it would seem desirable that more careful clinical studies and more exhaustive laboratory examinations should be made in those cases of polyarthritis in which tuberculosis past or present can be demonstrated with a view to clearing up this at present decidedly controversial subject.

1600 PROFESSIONAL BUILDING

DISCUSSION

DR. J. ALBERT KEY, ST. LOUIS, MO.—Chronic progressive monarticular arthritis in the child is considered tuberculous arthritis until it is proved otherwise. I have never been concerned about the early diagnosis of tuberculous arthritis. Dr. Dickson stresses the early diagnosis. I do not think it matters whether a tuberculous joint is diagnosed this month, next month, or next year, and the reason is this: In this country I have not seen a single instance where a large weight-bearing joint which was tuberculous was cured with useful motion. I am concerned not with the early diagnosis, but with the positive diagnosis. Just as soon as I am sure that the joint is tuberculous, I make it my purpose to eliminate that joint by arthrodesis. That is the only way I know by which the patient can be cured of tuberculosis. If you get a good bony ankylosis he is cured. If you cannot, the patient has a tuberculous joint as long as he lives.

There are only two ways of making the diagnosis in the early stage. One is aspiration and injection into a guinea pig. I think Dr. Dickson is right about subcutaneous inoculation. I have always used intraperitoneal injection, and I have had two negative guinea pigs from a joint which later was proved to be tuberculous. The other is biopsy. I have looked at a good many synovial membranes, and when I find a typical tubercle I think it is tuberculosis. When I do not find typical tubercles, I do not know. The thing to do is to treat the case expectantly. That is hard because most of these cases are in children and most of the parents want you to cure the child. You have to have a pretty intelligent parent to allow you to treat the patient expectantly until you are sure it is tuberculosis. If it is tuberculosis, the next thing to do is to pick a time to operate on the child or adult.

The most important thing in my mind in the diagnosis of tuberculosis is the differentiation of a tuberculous joint from a pyogenic joint, strange as it may seem. If you operate upon a fulminating tuberculous joint and try to do an arthrodesis, you are likely to get into trouble. I have done it twice and both patients died, one before amputation and one after. We can get all gradations in a tuberculous joint from a simple synovitis with practically no thickening of the synovial membrane and negative x-ray which may persist over a period of years to a fulminating joint which is hot and exquisitely sensitive. The usual type is the one that is moderately sensitive with a doughy feel, a thickened synovial membrane, and not much fluid in the joint.

I have performed synovectomy on two occasions for rheumatoid arthritis, and when I got into the joint I still thought it was rheumatoid arthritis but when the sections came through I found it was tuberculosis. The symptoms recurred in a few months and we did an arthrodesis. On another occasion I drained an acute elbow for a presumably pyogenic infection and the sections showed tuberculosis.

Concerning the tuberculous rheumatism of Poncet, as I recall that is a tuberculosis without tubercle bacilli and without tubercles. I have been looking for this disease for a number of years, and I have never seen a case and do not think it exists. I think Poncet was a man who was seeing rheumatoid arthritis, but was so hipped on tuberculosis that he called his rheumatoid arthritis tuberculous arthritis.

DR. EDWIN W. RYERSON, CHICAGO.—Yesterday I saw in Billings Hospital of the University of Chicago with Dr. Phemister a case of such interest that I want to report it.

A woman of fifty odd years was lying in bed, with typical severe, old arthritic manifestations with which we are so familiar. Her hands, elbows, and knees were swollen. She had been that way for years. A few weeks ago both elbows developed swelling just above the joint. Phemister cut into both of these and proved they were tuberculous. Whether this was Poncet's tuberculous rheumatism or not I do not know. After some investigation they found a tuberculous process in the neck.

I have seen two proved cases of pneumococcus arthritis in the joint, one in a child and the other in a woman. After evidently proving they were pneumococcus, they ran a prolonged course and were later found to be tuberculous without tuberculosis in any other portion of the body. I think Dr. Dickson's paper is timely, because all of us are faced by joints which appear to be arthritic and later proved to be tuberculous. The converse is also true. Years ago I saw a young woman with a knee joint which to Dr. Capps and myself

seemed to be tuberculous. Several tuberculin tests were negative. Finally the synovial cartilage was found to be definitely damaged and the knee became perfectly well after the removal of this cartilage.

DR. FRANK D. DICKSON (closing).—I was once young and dogmatic like Key. Had I been writing this paper five years ago, Dr. Key would not have discussed it in the way he did, because I would not have said what I did. The experience of years, however, has caused me to hold different opinions from what I have held in the past. For example, it so happens that I have had under my care three cases of synovial tuberculosis of the knee, fairly well proved and cured with function. One of these cases, a boy, rowed on the Princeton crew several years ago, which would indicate a pretty satisfactorily functioning knee. I had this patient under observation from the time he was a young boy; moreover, during the course of his disease he was seen by other surgeons, and the diagnosis of tuberculosis was confirmed. Girdlestone reports a very recent series of early cases of tuberculosis recovered with function. These cases were carefully diagnosed and very carefully checked up. Girdlestone believes from his experience that we are not getting better results in early cases of joint tuberculosis because we are not recognizing them early enough and not keeping them at rest long enough. I believe that this is a theory which is worthy of our thoughtful consideration and one that should be given a thorough try-out. It is my conviction that there has been a small but definite percentage of tuberculous joints in which the diagnoses were made early which have recovered with function. If a tuberculous joint is seen in a child of two or three years of age, you are not going to fuse that joint; you must treat it conservatively until such a time as you can do a fusion successfully, say until the child has reached the age of six or seven years. Why is it not worth while then to make an early diagnosis and carry out treatment thoroughly and carefully during the period of waiting until fusion can be done, as we may once in a while with this method secure healing with function?

DIFFERENTIAL DIAGNOSIS OF GONOCOCCAL ARTHRITIS*

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GONOCOCCAL arthritis differs in the main from the large group of arthritides classified as infectious arthritis only in that the etiologic agent is known and can be identified in suitable cases. There is probably one major clinical syndrome characterizing this disease which is of any diagnostic importance aside from the discovery of the gonococci in the joint or synovial fluid and that is the rapidity with which the acute process and the atrophy of the bone and muscle and tendon structures progress.

Significant factors in establishing the diagnosis are as follows: a history of exposure followed by a yellowish discharge three to twenty days later accompanied by the sequelae of painful urination, etc. Involvement of the prostate or tubal structures may follow the onset of this discharge by a very few days or weeks or months, and coincidental with this or at some later date any joint or group of joints may develop symptoms of acute disease. Careful history usually reveals transitory involvement of many joints at the onset over a period of several days, followed by the acute major involvement of one (commonly) but not infrequently several joints or near-by structures. It is not unusual for the involvement of one joint to subside and the process to flare up successively in other joints. It is not infrequent for the major damage to involve a joint traumatized previous to infection.

Physical examination shows usually a bluish red, hot, tender joint not very different in appearance from that due to a nonspecific joint involvement except that it produces unusually severe symptoms. The process may, however, be restricted in some cases entirely to the tendon sheaths or bursae around the joint or the muscle and fascia near by. The atrophy described above progresses rapidly from the onset.

Examination of the discharge from the genitourinary tract may show positive smears in about 40 per cent, positive cultures in about 60 per cent of all suspects although in our experience in these acute cases the smear and cultures are usually positive. Cultures of the material from the joint, bursae and tendon sheaths in the early acute stages yield growth of gonococci in 80 per cent of the cases. Later in the disease, the joint fluid is usually sterile to ordinary cultural technic. Complement fixation tests on the blood are negative for from two to six weeks following onset of the infection. It may require from four to twenty weeks for complete fixation to occur. When the patient has recovered, a complete fixation may become less fixed (i.e., negative) within six to eighteen months, although some may still be positive four years

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after recovery. Less strong reactions may subside very quickly depending upon the extent of the reaction. Skin tests with toxic material from the gonococcus are still in the experimental stage, but may be significant if that material is freshly made. The toxin of the gonococcus produces an erythematous reaction in the skin in the absence of the disease.

In the absence of history of exposure and negative smears and cultures, the positive blood complement fixation test is probably a very significant aid in the diagnosis. We suggest making this test on the joint or bursa fluid also, although any body fluid is probably positive in active cases. With a previous history of infectious arthritis, and a recent gonococcal infection with flare-up of a joint, the situation is very complicated. A nongonorrheal arthritis may flare up due to the intoxication arising from the gonococcal infection without gonococcal invasion in the joint. On the other hand, joints which are already damaged probably offer fruitful soil for the gonococci which are circulating in the patient's blood. The acuteness of the reaction and the rapidity with which the joint surfaces are damaged and the rapid onset of the atrophy, far out of proportion to the changes which usually accompany ordinary arthritis, are suggestive points in differential diagnosis. The diagnosis, of course, cannot be established clearly without the cultivation of gonococci from the joint or synovial fluid.

The manner in which the cultures are made is of vital importance, the bacteriologic technic determining the success or failure of the diagnosis in many cases. In women, cultures should be taken from the discharge from the cervix during the last two days of and the two days following the cessation of the catamenia. In males without discharge, after careful prostatic or urethral gland massage, the urethra should be washed out with sterile saline which should be cultured.

The radiographic appearance of the joint in acute gonorrheal arthritis has no outstanding characteristics except perhaps the unusual, diffuse character of the atrophy and the tremendous extent of the bone destruction considering the short duration of the disease. Chronic cases show no peculiar characteristics unless it be the extreme deformity and capsular thickening. This is not commonly found in the usual case of infectious arthritis. Where a growth of the gonococcus is not obtained from the joint fluid and in the absence of good history of gonococcal infection, the patient should be investigated for brucellosis, tuberculosis, typhoid, syphilis (secondary), and low-grade staphylococcus and streptococcus infections. On failing to demonstrate any of these, the diagnosis by exclusion is probably infectious arthritis (nongonorrheal).

The fallopian tubes may be sealed off and act as foci for years in the absence of evidence of disease in the lower birth canal. The complement fixation test is of assistance here. Chronic prostatitis with occasional yellowish discharge or bleeding after urination may be due to a small residue of gonococci. Old infected strictures and glands in the urethra of both sexes and Bartholin's glands may act as foci. Secondary invaders left as residual foci may help in setting up the syndrome of nongonorrheal infectious arthritis in the patient

debilitated by a severe gonococcal infection of the genitourinary tract. Such secondary invaders may persist for months or even years.

Spontaneous remissions of gonorrheal arthritis may occur without much residual damage in a fair percentage of cases. Upon reinfection of the genitourinary tract by gonococci the previously damaged joint or joints are likely to be involved first. In occasional cases such a joint is not involved at all, but one or several other joints become painful and show various degrees of involvement.

The febrile reaction is usually a mild one in gonococcal infections (1°-2° C.) but the pallor and intoxication and prostration are excessive. Electrocardiographic changes (prolonged P-R interval up to 0.21 second) occur in about 5 per cent of all cases. These subside later and are probably due to the gonotoxins. The extreme dysfunction of the quiescent joint may be due in part to the destruction of its surface, but in general is due more to the inflexible connective tissue granuloma infiltrating the capsule and other structures surrounding the joints, bursae, tendons, muscles, etc., concerned.

DISCUSSION

DR. C. B. FRANCISCO, KANSAS CITY, MO.—I think this has been a very fair discussion and a very fair presentation of the problem. I tell the medical students that gonorrheal arthritis is one thing that they need to know the clinical symptoms and story of, for the reason that no matter how carefully the laboratory work is done there is a large percentage of cases that cannot be proved by laboratory methods the first time. I use that to illustrate the point that clinical medicine is ordinarily likely to be sufficient. The findings and a positive history or the finding of the gonococcus are positive proof, but it is very difficult to get a proper history. Then you have to be pretty tactful about it. There are some cases where we are better off not to attempt to get a history because we will get into trouble, and get into more trouble by trying to insist. There are other cases in which I think it is quite important to go into the history because the patient wants you to ask him about it. They know about it, and they think unless you discuss this question with them that you will not know what is the matter with them. It is very fine handling of a case to know how to approach the subject. It is one I have not quite solved.

The clinical symptoms are quite characteristic. The extreme pain without much prostration and without much loss of weight is quite characteristic when preceded by this floating type of joint involvement. I had a patient who had osteomyelitis as a youngster, and four years later he was unfortunate enough to contract gonorrheal arthritis. He told me there was no comparison between the pain of osteomyelitis and the pain of the gonorrheal arthritis. The pain is severe and it is extreme, and yet these patients do not lose a lot of weight. Their general condition remains very good. The appetite is good and they do not have much fever.

I think that helps in diagnosing a case. To me it is rather sad that there are so many doctors to whom it does not occur that the case is one of gonorrheal arthritis. They start in on the theory that it is something else, like focal infection. A good many joints are ruined because it never occurred to the doctor that it might be gonorrhea.

I should say the most important point in diagnosis is to think about it. You never diagnose a thing that you do not think about, no matter how trivial the case may be. Consideration of it, a rather careful history, tactful management in getting the history, and the picture as it proceeds will lead one to make a diagnosis. Of course the laboratory technic should go right along.

DR. J. ALBERT KEY, ST. LOUIS, MO.—Gonorrheal arthritis usually begins as an acute arthritis, but not always. We see chronic low-grade synovitis which is not very pain-

ful and is due to gonorrhea. We also see, and this is the group I am trying to separate out at the present time, chronic polyarthritis which is due to the gonococcus, but clinically is rheumatoid arthritis.

I want to bring out the use of fever therapy in the diagnosis of gonorrheal arthritis. Most cases of gonorrheal arthritis are cured by fever therapy. If you take a patient with arthritis of unknown etiology and put him in a cabinet, raise the temperature to 106° or 107° for four or five hours and he gets well, that is good evidence that the case was one of gonorrheal arthritis. I think in the future we will submit certain of our patients to fever therapy as a diagnostic procedure, and if the arthritis is due to the gonococcus, that case will be cured by the test.

DR. MAURICE F. LAUTMAN, Hot Springs National Park, Ark.—Dr. Warren has correctly stressed the point about the ease with which the acute type of gonorrheal arthritis can be diagnosed. However, the differential diagnosis between gonorrheal arthritis and ordinary atrophy or rheumatoid arthritis is at times quite difficult, particularly if non-gonorrheal foci of infection are present. In the zeal for eradicating the obvious infective foci, the possibility of a concomitant, postgonorrheal infection is frequently overlooked. In our experience, examination of the prostate and prostatic secretion has given us a great deal of information. I was sorry not to have heard Dr. Warren stress that point. The cultural findings are usually negative, particularly if the arthritis occurs long after the original infection. There are more or less typical subacute cases of gonorrheal arthritis in which the prostatic smears are negative bacteriologically. In these cases the only finding to which we can attach any importance is the finding of pus cells in the prostatic secretion, particularly by examining the fresh secretion under the high power field. The finding of ten or twelve cells per high power field is enough to incriminate the prostate as a focus of infection, but the finding of gonococcus, either in stained specimens or in cultures, is necessary to definitely establish a gonococcus foundation for the arthritic findings.

DR. STAFFORD L. WARREN (closing).—First of all, I would like to answer Dr. Key that fever therapy is not a diagnostic procedure. What will you do with known strains of gonococci that will stand forty hours of heating at 41.5° C. and will not be cured by short fever treatments?

About the prostate, I meant to infer that secondary invaders may be left, that the gonorrhea may be gone and yet the prostate be the focus of infection in the arthritic condition. I think some of these chronic prostatic cases under ordinary conditions still harbor gonococci, and one may demonstrate them if a concerted search be carried on and especially if the oxydase test is used to identify the one or two colonies which you might miss on a plate because the plate is crowded with streptococci, staphylococci, and colon bacilli.

THE DIAGNOSIS OF GOUT AND GOUTY ARTHRITIS*

PHILIP S. HENCH, M.D., ROCHESTER, MINN.

ONLY one of four or five cases of gout is correctly diagnosed in its early stages. But in some quarters only one of two or three patients who receive a diagnosis of gout actually has the disease. Thus are reflected two attitudes: that of the conservative who hesitates to make a diagnosis of gout except in the presence of tophi or chronic hyperuricemia or both, and that of the liberal who considers chronic arthritis with transient hyperuricemia, or certain gastrointestinal symptoms of a bon vivant, or even Heberden's nodes, as bona fide manifestations of gout.

Requirements of different physicians for a diagnosis of gout vary. Of the two extremes, the overly conservative viewpoint is now more frequent. Hence, many cases of gout are masquerading under the diagnoses of rheumatic fever or of atrophic, hypertrophic, or traumatic arthritis. Foci are removed and vaccines are given, but the patients continue to suffer because their physicians never think of gout, or dismiss it as a disease that is extinct or one which their well-mannered patient "just couldn't have." This attitude permitted my observation that in 100 cases of gout an average of fifteen years had elapsed from the first attack of gouty arthritis to the first diagnosis of gout.[1] The necessity of taking 1,500 years to diagnose 100 cases of classical gout does not indicate a proper understanding of this disease.

The advertized features of gout are podagra (painful great toe), hyperuricemia, roentgenographic evidence of erosion and tophi. Textbook definitions have fostered the idea that the great toe is affected in practically all cases, that a short time elapses between toe and tophus, that an elevated value for blood uric acid is a consistent, persistent feature, and that pathognomonic roentgenographic changes appear fairly soon. To evaluate the diagnostic worth of these and other features, a study has been made of several hundred cases of gout: cases of tophaceous gout about which there could be no question, and cases of pretophaceous gout, similar to the former in every regard except that discoverable subcutaneous tophi had not yet appeared.

"Gout" and "gouty arthritis" are not synonymous. There is much more to gout than its articular manifestations which, however, produce the dominant symptoms. The evolution of gouty arthritis is as follows (Fig. 1): The first attack usually appears after the age of forty years. Its onset is sudden. It generally lasts only three to seven days and then disappears completely. A large toe, or with almost equal frequency, another joint, may have been affected: an instep, heel, ankle, or knee. After a year or two another attack appears, often more severe and of perhaps seven to fourteen days' duration.

*From the Division of Medicine, the Mayo Clinic.

Abstract of paper read at the Third Annual Meeting of the American Association for the Study and Control of Rheumatic Diseases, Kansas City, Mo., May 11, 1936.

It, too, disappears without articular residue. Sooner or later the disease increases in tempo and severity, attacks coming every few months. At first attacks are generally monarticular, have little tendency to invade another region; later attacks may be frankly polyarticular, another region being affected as one recovers. Certain characteristics of the individual attacks are almost pathognomonic of gout, as will be shown later, but the one of greatest diagnostic import (aside from the actual discovery of tophi) is that after a variable number of days or weeks the fairly short attacks of acute arthritis disappear with no symptomatic residue.

Five to forty years (average twelve years) after the first attack an important change occurs: joints no longer recover completely; disability may become chronic. Thus is initiated the second stage of articular gout, that of chronic gouty arthritis. In this stage the joints at first are subject to acute exacerbations with incomplete remissions. Finally, exacerbations cease and the patient presents misshapen extremities with multiple tophi, yet the joints are relatively painless.

THE BASIC PATTERN OF GOUT AND GOUTY ARTHRITIS (UNTREATED)

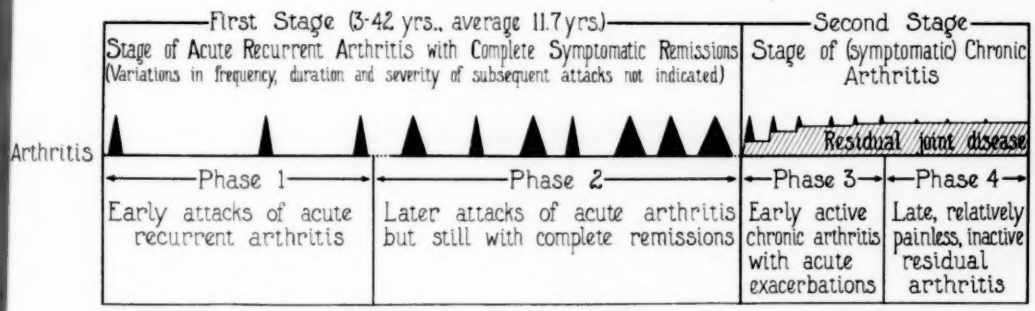
First Stage (3-42 yrs., average 11.7 yrs.)
Second Stage
Stage of Acute Recurrent Arthritis with Complete Symptomatic Remissions
(Variations in frequency, duration and severity of subsequent attacks not indicated)
Stage of (symptomatic) Chronic Arthritis
Arthritis
Residual joint disease
Phase 1
Phase 2
Phase 3
Phase 4
Early attacks of acute recurrent arthritis
Later attacks of acute arthritis but still with complete remissions
Early active chronic arthritis with acute exacerbations
Late, relatively painless, inactive residual arthritis

Fig. 1.

Thus, the course of gouty arthritis can be divided into two great stages, each consisting of two phases: Stage I is that of acute, recurrent gouty arthritis with complete remissions (Phase 1 is that of early attacks; Phase 2, that of later acute attacks with remissions, when hyperuricemia is likely to be more established and discoverable). Stage II is that of chronic gouty arthritis (Phase 3 is that of early chronic gouty arthritis with acute exacerbations but incomplete remissions; Phase 4, the final, relatively symptomless, chronic gouty arthritis). Thus the pattern of gouty arthritis is so distinctive as to be almost pathognomonic. Tophi are the one pathologic proof of gout. Depending on the presence or absence of discoverable tophi, one will make a diagnosis either of tophaceous gout with acute recurrent gouty arthritis or with chronic gouty arthritis, or a diagnosis of presumptive (pretrophaceous) gout with acute, recurrent gouty arthritis or with chronic gouty arthritis. A patient with mild or slowly progressive gout may die of some other cause before ever reaching the third or fourth phase of gout. Of 100 cases of gout seen at the clinic, about two-thirds were in Stage I, about one-third in Stage II.

Let us study the appearing time of the four advertized features of the disease. Unless they appear fairly early and fairly consistently, they are of

little help in early diagnosis, even though they may be of great help in the late diagnosis of gout. Podagra is undoubtedly a common, but not a consistent, feature of gout. In one group of 100 cases the initial attacks involved the great toe in about 60 per cent of cases; however, in the remaining 40 per cent the great toe was not affected. Whereas one patient had 30 attacks, in 20 instances a great toe being affected, another patient with a total of 150 attacks experienced only 10 in a great toe. One must therefore not hesitate to diagnose gout in the absence of podagra.

Let us note the evolution of hyperuricemia. The hyperuricemia of gout may at first be somewhat acute and transient; later it may be chronic. It may be present or absent during the initial or early acute attacks but is often absent between early attacks. In later attacks hyperuricemia becomes more obvious, more frequent and may persist between attacks. With chronic gouty arthritis, hyperuricemia is practically always present and, without treatment, is chronic.

Subcutaneous uratic tophi are rarely present before or during the first attack, are rarely seen in Phase 1, become more common in Phase 2 and are seen almost invariably in Stage II. A "tophus" is not a tophus until it has been removed and examined for urate crystals. A murexide test gives helpful confirmation. In certain situations urate tophi simulate the subcutaneous fibrous nodules seen in fibrositis and in atrophic arthritis. Histopathologic differentiation by the new method of Galantha[2] is usually desirable. At a given time a physician may find tophi in only about 40 to 50 per cent of his total cases of gout. Old tophi may ulcerate. Two diseases of joints may present periarticular fistulas: tuberculosis and gout. Since gouty arthritis is much commoner than tuberculous arthritis, a useful maxim is: Any ulcerating, periarticular lesion should arouse suspicions of gout.

Areas of erosion in articular or juxta-articular bone in gout represent osseous tophi, the replacement of bone by urate deposits. Probably present in every attack, they are generally too small to be visible in early attacks. They may occasionally be seen in later acute attacks; become increasingly numerous and large during the development of late gout. Small areas of erosion (masses of noncrystalline, nonuratic débris) are commonly seen in cases of atrophic and hypertrophic arthritis. Therefore, such areas are not pathognomonic, but if large, are usually attributable to gout. They practically never appear in gout except in roentgenograms of hands or feet; hence, too frequently roentgenograms in gout are "nonspecific," reveal "periarticular," "hypertrophic," or "destructive changes." When any of these characteristic features (podagra, hyperuricemia, tophi, erosion) are present, they are highly significant and their diagnostic value cannot be minimized, but if these features on which the diagnosis of gout has so generally depended are so variable in the time of their appearance, one must turn elsewhere for a more reliable basis for early diagnosis.

Most gouty patients who present themselves to the specialist in arthritis or to the clinic physician will already have had one or more attacks. Although tophi may not yet have appeared, the unfolding of a clinical pattern obviously characteristic of gouty arthritis permits a diagnosis of pretophaceous (pre-

sumptive) gout. Such a diagnosis can be entertained with no little assurance since the pattern described is practically distinctive for gout and is not exactly mimicked by any other form of arthritis. In atrophic arthritis the onset is generally insidious, the course chronic from the start, with many partial but practically no complete remissions. Even when the onset is acute or subacute the acute phase lasts not days (as in gout) but weeks or even months. Of seven "rheumatic diseases" other than gout, characterized by a tendency to acute attacks with more or less complete remissions, each has distinctive features that hardly permit confusion. These are rheumatic fever, intermittent hydrops, periarticular fibrositis, psoriatic arthritis, arthritis with ulcerative colitis or that with hemophilia, and recurrent subdeltoid bursitis. The graphs of clinical activity in none of them exactly simulate that of gout, and usually the parent disease provides a distinguishing mark for each.

If the patient is seen in his first attack and the characteristic clinical pattern of gouty arthritis has not yet developed, diagnosis must be based on certain features of individual attacks which, while not pathognomonic, are highly suggestive. They pertain to sex and age, precipitating factors, season, hour and speed of onset of attacks, speed of development, character and severity of the pain, situation of joints involved, vagrancy of the affection, appearance of the joints, site of maximal tenderness, duration of attack and obvious tendency to restitution of articular function. Of additional diagnostic importance is the frequent presence of certain renal lesions seen in mature cases of gout.

About 98 per cent of patients who have gout are males. A diagnosis of gout applied to a woman should be made with caution but can be based on the same features as those of gout in males. Gouty arthritis, uncommon before the age of thirty-five years, is the commonest form of acute arthritis among men more than forty and should be first thought of if gonorrhea and acute trauma are excluded. Individual attacks appear at any time of year, the majority in spring and fall. Although attacks may begin at any hour, they appear with sufficient frequency between 2 and 7 A.M. that the notation that a given attack appeared then is worthy of special deliberation. Unusual speed in onset and development of an attack is distinctive of gout. Few, if any, of the arthritides other than gout develop so abruptly and reach their maximum within one to two days. The pain of gout, sometimes mild or moderate, is often excruciating, beyond that of any other type of arthritis—which is a very suggestive point. When a great toe is affected in gout, the maximal tenderness is usually at its mesial aspect, not on the top, or on the bottom of the toe as in atrophic arthritis. The affected extremity is more frequently hot and bluish red than clammy, cold and bluish white as in atrophic arthritis. Shiny skin, definite edema, and desquamation of skin as attacks subside are often notable. In cases of late gout periarticular tophaceous deposits may create an asymmetrical swelling of joints which contrasts with the symmetrical fusiform appearance generally seen in atrophic arthritis.

Trauma will precipitate many types of arthritis. In gout, however, a nontraumatized joint may promptly share the affection with the joint in which the attack is incited by trauma. Other precipitating factors seem peculiar to gout. The physician must specifically hunt for them, however, as the patient

is generally unaware of their importance and may omit mention of them. When found, these precipitating factors are of considerable significance and helpful in diagnosis. (1) Gouty arthritis (not other types of arthritis) is prone to appear after dietary indiscretions but may affect vegetarians and teetotalers. (2) Gout is often precipitated by the trauma, exposure and dietary excesses of a fishing or hunting trip. (3) Whereas patients with atrophic arthritis are usually temporarily benefited during any postoperative regimen, acute attacks of gout are prone to develop within the first six postoperative days. (4) Quiescent gout of gout-susceptible patients may be activated by treatment of some coincident disease: by liver therapy for pernicious anemia, ketogenic diet for bacilluria, salyrgan for dropsy, ergotamine tartrate (gynergen) for migraine, insulin for diabetes. (5) Gout is more frequent with polycythemia and leucemia than mere coincidence allows.

Gout tends to involve extra-articular as well as intra-articular tissues; hence, the frequency of tendinitis and of olecranon bursitis. Since olecranon bursitis is much more common in gout than in atrophic or hypertrophic arthritis, the presence of, or a history of, olecranon bursitis should lead to a search for other features of gout. To define the limitations of visceral (non-articular) gout still is vexing. Physicians of widest experience now consider the majority of miscellaneous visceral symptoms experienced from time to time by gouty patients as either unrelated to gout, or at least incapable of being proved truly gouty, because urate deposits are never found in related tissues. Kidneys provide the great exception. Gouty nephritis and renal colic from urate stones or gravel are frequent manifestations of gout in Stage II, occasionally in Stage I. Because of their frequency in gout and their extreme rarity in atrophic arthritis, the maxim is useful: Suspect gout in acute or chronic arthritis with a history or findings of renal colic or nephritis. It must be remembered that pure urate stones and gravel cast no roentgenographic shadow.

Intelligent patients welcome the discomforts of an attack provoked for diagnosis. Such provocative tests are of limited value. Since susceptibility varies greatly from time to time, conditions must be ripe for the test. It often fails in cases of known gout. It must be carefully interpreted, else a positive test may be claimed when weather or another factor provokes what actually is an exacerbation of, for example, atrophic arthritis.

Most important, the therapeutic test is that which, regardless of the presence or absence of tophi, convinces the patient and his physician of the nature of his disease. If his previously troublesome affliction can be largely or entirely controlled by measures useful only in gout, the skeptic will be convinced. Under vigorous and proper treatment a man who has been severely crippled for days or even weeks may in a few days be able to get about painlessly. This illustrates the saying of Aretaeus: "A person subject to gout has won the race at the Olympic games during the interval of the disease."[3] This is a point of the greatest diagnostic significance.[4]

In conclusion it is the suspicion of gout, unfortunately not the disease, which has disappeared. Awareness of gout should again have a place in the thought of American physicians. Suspicions often can be confirmed by dis-

covery of the enumerated characteristics of gout. If these criteria are used, gout will assume not the incorrect position of false high frequency of a century ago, nor that of the false rarity of the present, but its rightful incidence, about 5 to 8 per cent of cases in an arthritis clinic. Most important, a group of patients who are suffering needlessly will be restored to a large measure of comfort and contentment.

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DISCUSSION

DR. L. MAXWELL LOCKIE, BUFFALO, N. Y.—Dr. Philip Hench has accomplished a great task to make physicians in America "gout conscious" again. So many have thought it was an extinct disease in this country. The summary which was given today was well done.

It seems that gout is more common in certain localities of the United States than in others. Around Buffalo and western New York State a fairly high percentage of gouty patients are seen in the average run of arthritic patients. In the greatest number, the diagnosis can be strongly suspected because they do present a typical history pattern. This is apparent after a very few minutes' conversation.

Tophi may or may not be present. The blood uric acid is above the normal range in the big majority. It is well for one to be suspicious of gout in all male patients who have arthritis in whom there is some evidence of kidney insufficiency. The sedimentation rate of the red blood cells is increased in some.

Concerning therapeutic tests no drug is so specific as colchicine, which acts so well to abate an acute attack. It has been observed that patients with gout are likely to develop an exacerbation if a high fat diet is given. With a change to a high carbohydrate diet, the symptoms subside in twenty-four to forty-eight hours.

DR. EDWIN P. JORDAN, CHICAGO, ILL.—I think Dr. Hench's criteria are very good. I believe he and I began to look for gout at the same time, and I have found it more frequently than I anticipated. I believe that would be the case anywhere in the country if people looked for it. I find gout quite a complicating condition, and I know less about it now than I thought I did at first.

I would like to ask Dr. Hench two questions. The first is, does he think gout may start in the second stage without an attack of acute arthritis? I have had patients who had exacerbations of arthritis which at the time answered all the other criteria of gout, but which did not let up between attacks. Second, does he think the few cases of gout in families are on a hereditary basis?

DR. M. HENRY DAWSON, NEW YORK, N.Y.—Since Dr. Hench's original paper several years ago we have looked very carefully for cases of gout in our clinic but only rarely have they been encountered. One, of course, sees more cases in private practice. However, I have wondered whether there may not be a geographic factor which may account for the varying frequency of gout in different parts of this country. It is well known that the incidence of gout varies greatly in different parts of Germany and Austria.

DR. R. GARFIELD SNYDER, NEW YORK, N. Y.—Dr. Hench has just presented an excellent and very timely paper, and I feel sure it will arouse renewed interest in this very difficult subject. I agree with Dr. Dawson that if we consider a high uric acid an indication of the presence of gout, then typical gout is relatively rare in New York City. I have only

seen four cases of true gout in the last five years, and only one case of tophi in fifteen years. In these four cases of gout over a period of five years, the uric acid figures varied between 3.5 mg. and 6.6 mg. per 100 c.c. of blood, but as a rule the uric acid remained between 3.5 and 5.0 mg.

I have seen a large number of cases in which, from the history and appearance of the patient, one cannot help suspecting gout. These patients have usually been on self-imposed diets with rigid restriction of red meats before coming for examination, and for that reason their blood uric acid figures are often within the normal limits. These I classify as atypical gout. Is it not reasonable to assume that a blood uric acid of 3.5 to 5.0 mg. in cases of this type is indicative of, or presumptive evidence of, the presence of gout? I would like to ask Dr. Hench what method he uses to determine the amount of uric acid, and what in his opinion is the lowest figure at which a case could be classified as gout?

I have seen a few cases in which an acute attack of gout has been induced by the consumption of an excessive amount of sweets. Has Dr. Hench had any similar experience, and how would he explain this phenomenon?

DR. J. ALBERT KEY, ST. LOUIS, MO.—I would like to ask Dr. Hench whether because a man has recurrent attacks of pain in the feet one should consider him a case of gout, or does he have other evidence? Naturally, since gout is so rare in the East and in St. Louis and is seen so frequently in Rochester, we suspect that most of his cases are not gout at all, but are merely patients with foot strain.

DR. RUSSELL L. HADEN, CLEVELAND, O.—I would like to mention a group of five or six patients who came in on the urologic service for prostatic obstruction. Four were immediately relieved by relief of the back pressure on the kidneys. Uric acid should be considered whenever prostatic obstruction is present.

DR. HENCH (closing).—When a patient comes to us with a history of a number of attacks of acute arthritis, with complete remissions, but who has reached the stage where his attacks last six, eight, or ten weeks, and when after a very few days of a regimen of value only in gout he is running around entirely free of pain, regardless of the presence or absence of tophi what else can we call it but gout? We have had this experience repeatedly, often with cases of tophaceous gout which I believe would be accepted as true gout even in New York or St. Louis.

The factor of heredity in gout is probably very important, but it is not of much help in diagnosing gout in our American patients, for it is rare to find one who knows of any gout in his family. Regarding age incidence, as Dr. Jordan says, gout does occasionally appear in young adults and from Europe come reports of gout in male children, but, in the majority of our cases, acute gouty arthritis first appeared after the age of thirty or forty years.

About 98 per cent of patients with gout are males. I believe that the fewer cases of gout in women included in any one series, the more accurate the diagnoses of gout probably are, and if an investigator states that many more than 5 per cent of his patients with gout are females, his criteria of diagnosis are open to question. He is probably overly generous with his diagnosis of gout. In one German series of about 300 cases, approximately 35 per cent of the patients were females. On analyzing the criteria used for diagnosis I found them to differ markedly from those commonly accepted. Gout occasionally does occur in women but, when it does so, its characteristics are essentially the same as those of gout in males, and the criteria for diagnosis are the same in both sexes. In several hundred cases of gout seen at the Mayo Clinic, only three patients with tophaceous gout and about fifteen with presumptive (pretophaceous) gout, were women. In each case the history was the same as that for males: recurrent attacks with complete remissions.

It is my experience that the course of gouty arthritis is rarely if ever chronic from its onset. Of 100 patients studied by me some years ago, two were of the opinion that their gouty arthritis had progressed in chronic fashion from the start, with no complete remissions. In the past nine years I have been unable to find other such cases. All of my gouty patients have had a (preliminary) series of acute attacks with complete remissions in

articular symptoms. Hence, I am now somewhat inclined to doubt the veracity of the histories given by these two patients and to believe that their memories may have been faulty or my questioning inadequate.

At the Clinic, a normal concentration of uric acid in the blood is considered to be less than 4 or 4.5 mg. per 100 c.c. (Folin method, 1930). As I have mentioned, many patients with early gout have a normal concentration of blood uric acid. It must likewise be remembered that there are other causes for hyperuricemia than gout. Quick recently summarized them as follows: states where ketosis arises, such as in fasting, in severe diabetes, and on a high fat diet; states where an excessive accumulation of lactic acid may arise, such as in eclampsia, chloroform poisoning, pneumonia, circulatory failure and various other conditions of anoxemia, or with lactic acid feeding; after ingestion of excessive amounts of sodium bicarbonate; in severe renal disease, and after administration of benzoic acid, phenylacetic acid and numerous other aromatic acids that decrease uric acid excretion. To this list should be added leucemia and polycythemia.

The presence of hyperuricemia in a case in which there is a history suggestive of gout is an added point in favor of such a diagnosis, but when the history is quite atypical for gout, we seek another explanation for a hyperuricemia. The patient's history may thus be more reliable than the test for hyperuricemia; and for the discovery of gout a most important leading question to an arthritic patient is this, "Has your arthritis ever cleared up entirely? If so, how often?" Answers to such questions are of great diagnostic importance.

In most series of carefully studied cases of gout, tophi have been found at any given time in only about 40 to 50 per cent. Just as the sex incidence in any one group of cases can be used as somewhat of an index to the correctness of an investigator's diagnostic criteria, so will the percentage incidence of tophi give a clue as to whether an investigator is too inclusive or too exclusive in diagnosis. If the great majority (75 per cent or more) of a physician's cases of gout have tophi, he is probably too exclusive in the diagnosis of gout and is missing cases of presumptive (pretophaceous) gout. If only a small percentage (25 per cent or less) of his patients have tophi, he is probably diagnosing gout where it does not exist. It is foolish, however, to insist on waiting upon pathologic proof (tophi) for a diagnosis of gout. If one is content with only a pathologic diagnosis, that is almost analogous to waiting for a stroke before diagnosing arteriosclerosis, or for a uremic convulsion to make a diagnosis of nephritis.

We have used the provocative (high fat, low carbohydrate diet) test for gout proposed by Lockie and Hubbard. It is a useful, but not a consistently positive, test, and it has not always given provocation in our cases of known gout. When definite provocation is obtained, unexplainable on other grounds, gout is present in all likelihood since this test diet does not seem to aggravate cases of atrophic or hypertrophic arthritis. It should be settled whether it is necessary to obtain ketosis before the diet will provoke gout. I have seen several cases in which unmistakable, acute gouty arthritis developed while patients were on a ketogenic diet for the treatment of urinary infection with colon bacilli. I cannot confirm Dr. Snyder's experience. I have not seen gout provoked by candy or other excess of carbohydrates. According to Lockie's experiments and the opinion of Quick, an excess of carbohydrates should benefit gouty patients and tend to prevent attacks. An exception might be the case of a patient with a double metabolic fault, one with gout and diabetes. When a gouty patient consistently fails to respond to a regular gout regimen, adhered to faithfully, experience has led me to hunt for some other metabolic disturbance complicating the gout, such as latent or unsuspected but active diabetes or an abnormality in thyroid function. I have studied several patients with both diabetes and gout in the past two years. One was a patient who was also seen by Dr. Lockie, a physician with intractable gout. Repeated sugar tolerance and other tests demonstrated the presence of a definite but subsymptomatic diabetes. When treatment for the latter was given, the management of the gout was more successful.

DIFFERENTIAL DIAGNOSIS OF PERIARTICULAR FIBROSITIS AND ARTHRITIS*

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INCIDENCE

FIBROSITIS is the commonest form of acute or chronic "rheumatism." Almost everyone suffers once if not oftener with it at least in its mild, subacute form. Statistics of the British Ministry of Health show that of 2,500 insured persons who were affected in one year with one of the rheumatic diseases, 60 per cent had some form of fibrositis. In spite of its wide recognition abroad and great prevalence everywhere, it has received scant attention in this country.

ETIOLOGY

In most cases of fibrositis the exact cause is not known; trauma or exposure to thermal changes sometimes precipitates or causes attacks. Gonorrhea, gout, rheumatic fever and atrophic arthritis often affect extra-articular and periarticular tissues more readily than intra-articular structures and produce special types of fibrositis. In most cases, fibrositis is believed to be attributable to some unidentified infection or toxin.

CLASSIFICATION

On supposed etiologic grounds, fibrositis can be tentatively classified thus: (1) Primary fibrositis is unaccompanied by, and independent of, any other definite disease and presumably is attributable to an unidentified infection or to toxemia. This is the common type, nonspecific (perhaps infectious) fibrositis; it is the type generally meant when the term "fibrositis" is used. (2) Secondary fibrositis is secondary to some known cause or primary (dominant) disease such as: trauma, gonorrhea, rheumatic fever, gout, senescent (hypertrophic, osteo-) arthritis, infectious (atrophic) arthritis, a variety of diseases such as influenza. This inadequate groping for order indicates that knowledge of the clinical features and pathology of fibrositis is even less complete than is that of several other types of "rheumatism."

Only primary fibrositis will be mentioned in this abstract; in the complete paper space will be given to secondary fibrositis.

PRIMARY FIBROSITIS

Anatomic Types.—On anatomic grounds primary fibrositis may be classified thus: (1) intramuscular fibrositis, "myositis" or "muscular rheumatism"; (2) periarticular (capsular) fibrositis, "capsular rheumatism"; (3) bursal fibrositis,

*From the Mayo Clinic.

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"bursitis"; (4) tendinous fibrositis, for example, the palmar fibrositis that may lead to Dupuytren's contracture; (5) perineural fibrositis, of which "sciatica" or "brachial neuralgia" are common types; (6) panniculitis.

Considering differences in situation, it is obvious why symptoms and signs of the anatomic varieties of fibrositis differ considerably although the varieties are united by a common pathologic basis.

Pathology.—In Stage 1 there is an inflammatory, serofibrinous exudate of low grade, with proliferating fibroblasts and newly formed blood vessels. In Stage 2, if the inflammatory process is more severe and of longer duration, indurated, local, tender, thickened tissue or frank, gross, subcutaneous nodules may be produced. They may become firm and in them may be found dense inflammatory hyperplasia of fibrous tissue, thickened blood vessels and inflamed nerve fibrils. There is no leucocytic reaction. In Stage 3, when the inflammatory activity has passed spontaneously, or as the result of treatment, some indurations may disappear. Others remain as painless thickenings or nodules. Fibrous, tendinous contractures, capsular thickenings may affect such joints as the shoulders and palms.

Intramuscular and Periarticular Fibrositis.—These are the two common, anatomic varieties of fibrositis. About half of my patients who are affected by primary fibrositis have both intramuscular and periarticular fibrositis, a fourth have periarticular fibrositis only and a fourth have intramuscular fibrositis only.

Intramuscular fibrositis produces symptoms between, not at, the joints. It may appear as lumbago, torticollis, pleurodynia, or cephalgia or may affect muscles of groups other than those designated by the terms just used.

Periarticular (capsular) fibrositis (capsular rheumatism) is much too commonly mistakenly diagnosed as arthritis. At first there may be little or no pain when joints are at rest or in moderate use. Pain or stiffness may be noted only during the first few movements on awakening, or after the joints have not been used for a while, or when the joints are used excessively, or when the capsule is stretched. The patient may have to hunt for soreness by twisting the joint sidewise, squeezing it or flexing it forcefully to convince himself of the actuality of and of the situation of pain. After a short experience with these rather intangible symptoms, the patient may note their gradual disappearance.

If the disease progresses, pain becomes more constant, chronic aching may appear and tenderness becomes less elusive. Joints feel stiffer, yet relatively full, although painful motion may still be readily accomplished. Generally definite swelling or hydrops do not appear. However, capsular thickening may appear. Usually there is little, if any, redness or significant muscular atrophy and the roentgenograms represent a normal condition. It may be difficult for the patient to limber up on waking. Setting-up exercises, a hot bath, or acetylsalicylic acid may be required to produce sufficient limberness. Damp or cold weather may make the stiffness and aching worse. Marked fatigue and nervous exhaustion may appear. In spite of these symptoms, physical examination may not disclose anything essentially abnormal. Sometimes gross fibrous nodules are found over the elbows, knuckles, or about the gluteal, sacro-iliac or occipital regions.

These symptoms may be present for a few days or weeks, for months or years. Vagrancy and variability in the intensity of symptoms are characteristic, much more so than in atrophic arthritis.

Generally the affection disappears eventually, leaving no deformity of joints. When contractures and deformities do occur, they result from periarticular and not from intra-articular disease.

DIFFERENTIAL DIAGNOSIS OF PERIARTICULAR FIBROSITIS AND ARTHRITIS

In this paper the differentiation of periarticular fibrositis from arthritis will alone be considered further.

In the absence of direct pathologic proof, abundant indirect evidence demonstrates the persistent integrity of the joint cavity in cases of fibrositis. In periarticular fibrositis the disease is at the joint, not within the joint. In infectious arthritis, however, there is fibrositis plus synovitis, chondritis, and osteitis.

Clinical Differential Diagnosis; Comparative Symptomatology.—Periarticular fibrositis and atrophic arthritis have several features in common: incidence by age, manner of onset (acute or chronic), relative incidence by sex, bodily types affected and prodromal symptoms (fatigue, chilliness, nervous exhaustion). However, certain other features are sufficiently characteristic of each to be helpful in diagnosis.

Joints: The clinical course of periarticular fibrositis differs from that of atrophic arthritis. In atrophic arthritis there is a tendency to polyarticular invasion. In periarticular fibrositis, although many joints are sometimes affected, often only one or two large joints or several small joints are affected. Articular tenderness is to be expected in cases of atrophic arthritis; in periarticular fibrositis, generally little or no tenderness is present.

In atrophic arthritis stiffness of joints is generally objective as well as subjective; in periarticular fibrositis it is frequently only subjective. The symptom of "jelling," stiffness of a joint during rest, may be the first or only symptom. Atrophy of muscles is commonly seen in cases of atrophic arthritis but is generally absent in periarticular fibrositis.

In atrophic arthritis three factors produce the appearance of articular swelling: (1) hydrops from the synovial reaction; (2) fibrous thickenings of periarticular tissues; and (3) atrophy of muscle. In periarticular fibrositis there may be slight thickening of periarticular fibrous tissue but factors 1 and 3 are absent; hence swelling is not notable.

Motion of affected joints usually causes pain to patients who have atrophic arthritis. In periarticular fibrositis there may be no pain on ordinary motion but pain may be present with unusual, forced or lateral motion which stretches the capsule. Arthritic joints often feel worse after moderate exercise. Joints affected with fibrositis are frequently subjectively better after moderate exercises. They may hurt only the first few minutes of the day and feel all right thereafter.

In atrophic arthritis there are few complete remissions or even complete intermissions in symptoms. Although symptoms vary in intensity there is generally a constant minimum of discomfort. In periarticular fibrositis, complete remissions, particularly short, complete intermissions are frequent. Patients

who have periarticular fibrositis experience much more marked variability in intensity and persistence of symptoms than do those who have atrophic arthritis. However, fibrositis may produce symptoms that remain chronic for a long time. In atrophic arthritis there is little or no tendency to migration of symptoms. In periarticular fibrositis different joints are often involved in successive bouts.

Systemic Manifestations.—Atrophic arthritis is a disease of joints attended by many systemic manifestations. Common findings are slight fever, subnormal cutaneous temperature, tachycardia without fever, lowered blood pressure, anorexia and significant loss of weight. In periarticular fibrositis these are usually absent.

Fatigue and nervous exhaustion are frequent attributes of both diseases, but in atrophic arthritis they are often submerged, since the patient does not exert himself much. Patients who have periarticular fibrositis are usually quite active in spite of their pains, however; hence fatigue and nervous exhaustion are generally marked and often are notable for being decidedly out of proportion to the objective evidence of disease.

Weight: Sixty-two per cent of patients who had arthritis lost weight; 47 per cent of them lost more than 10 pounds (4.5 kg.). Only 7 per cent of those who had fibrositis lost more than 10 pounds.

Roentgenographic Alterations.—Of the 100 patients who had fibrositis, 78, who had suffered a total of two hundred and eighty-four years of their disease, presented no intra-articular roentgenographic alterations, although 37 patients were forty-five years of age or older. In 22 per cent of cases there were hypertrophic changes, generally slight, interpreted as evidence of coincident, unrelated, senescent arthritis, since most of the patients were between fifty and sixty-six years of age. Roentgenograms of some patients were negative after ten to twenty-five years of periarticular fibrositis.

In contrast, in 86 per cent of cases of atrophic arthritis there was definite roentgenographic alteration. Although half of the 100 patients had had their disease less than a year, only 14 per cent of the entire group gave negative roentgenograms.

In a given case any intra-articular roentgenographic alteration speaks at once for arthritis (with or without fibrositis). If roentgenograms are negative for six to twelve months, without other definite signs of arthritis, one may favor a diagnosis of periarticular disease. In a case of short duration in which roentgenograms are negative, other data must be relied on for differential diagnosis.

Laboratory Differential Diagnosis.—Regard for clinical differences permits accurate differential diagnosis without recourse to the laboratory when symptoms have occurred for months or years without objective evidence of intra-articular disease. In the early weeks of a given case, however, differential diagnosis is not easy. Laboratory data may then be helpful. One hundred cases each of fibrositis and of atrophic arthritis were studied; cases were selected only to insure that enough early and late cases of each would be analyzed. In the cases of fibrositis the disease had lasted from four weeks to forty years; in arthritis, from three weeks to eighteen years.

Sedimentation Rate of Erythrocytes: The greatest laboratory differences were observed in estimations of the sedimentation rates of erythrocytes. In cases of fibrositis, the average sedimentation rate (at the end of an hour) was 11.6 mm. The rate was normal in 73 per cent, but slightly altered (16 to 25 mm.) in 16 per cent, significantly altered (25 to 32.5 mm.) in only 11 per cent. The rate was never more than 32.5 mm. Of patients who had rates of more than 20 mm., all but one had had fibrositis more than one year, most of them more than five years.

In contrast, the average rate in cases of atrophic arthritis was 71.5 mm. Although 25 per cent of the arthritic patients had had their disease less than six months, only 3 per cent had normal rates. Only 6 per cent had rates between 16 and 25 mm.; 91 per cent had rates of more than 25 mm. In 67 per cent of cases the rate was more than 50 mm., and in 23 per cent it was between 100 and 150 mm.

In atrophic arthritis altered rates were generally noted early, even within the first three to six weeks of the disease. Among six patients who had fibrositis of six months' duration or less, only one had an elevated rate (23.5 mm.).

Blood Counts: Little or no help in differential diagnosis is obtained from total leucocyte counts or erythrocyte counts. Estimation of hemoglobin gives clearer evidence of anemia. In the blood of only 5 per cent of patients who had fibrositis was the concentration of hemoglobin less than 13 gm. and in that of only one (a patient who had menorrhagia) was the concentration less than 12 gm. In 42 per cent of patients who had arthritis the concentration of hemoglobin was less than 13 gm. and in 19 per cent, less than 12 gm.

Combination of Abnormal Findings.—Elevation of the sedimentation rate and reduction in erythrocyte count, alterations in concentration of hemoglobin or in weight, are, of course, not specific for these two diseases. Hence, a patient who has periarticular fibrositis might exhibit one of these alterations because of some cause other than his rheumatism. It is well, therefore, to note that of the 100 cases of fibrositis, in 90 there were either none of these alterations or only one alteration. Those exhibited by the remaining 10 patients were practically never sufficiently impressive to be definitely misleading. In contrast the majority of the patients who had atrophic arthritis exhibited two or more alterations that were not slightly, but definitely, abnormal.

In a given case, therefore, if there is only one slight abnormality in laboratory findings, too much significance must not be attached thereto. It may be the basis of a guarded, tentative diagnosis of arthritis rather than of a final one of fibrositis. When in doubt, however, I favor making the tentative diagnosis of fibrositis rather than making a more pessimistic appraisal of the condition and running the risk of making a diagnosis of "arthritis" in a case in which it probably does not exist.

SUMMARY AND CONCLUSIONS

In any given case, then, the differential diagnosis between periarticular fibrositis and atrophic arthritis is based on a survey of certain direct and certain indirect evidence for or against the presence of intra-articular disease. Direct evidence in favor of intra-articular disease is afforded by the appearance of

synovial hydrops, and of roentgenographic evidence of disease. Less direct evidence is afforded by the appearance of the joints; notable redness, tenderness, muscular atrophy and definite swelling speak in favor of arthritis, as opposed to disease that is exclusively extra-articular.

Indirect evidence is afforded by a history characteristic of one or the other type and by certain laboratory data, particularly the sedimentation rates of erythrocytes and the estimation of hemoglobin. The weight curve also is significant. Alterations in these data particularly in two or more factors, beyond a certain maximum generally seen in cases of fibrositis speak against uncomplicated fibrositis and in favor of intra-articular disease.

The differential diagnosis in favor of periarticular fibrositis is made on the persistence with which direct and indirect evidence of intra-articular disease remains absent. When objective changes, systemic manifestations and alterations in laboratory findings known to be relatively consistent in cases of atrophic arthritis remain persistently absent, the arthralgia, stiffness and articular thickening can be, with no little confidence, ascribed to periarticular fibrositis and the fear of impending arthritis can be laid aside.

DISCUSSION

DR. PHILIP S. HENCH, ROCHESTER, MINN.—If gout in America is a forgotten disease, fibrositis is an unknown disease, at least it is not known by that name. The disease is very widespread in both England and America, but very little is written about it in this country and the term "fibrositis" is practically unrecognized here. In the three "F" volumes of the Surgeon General's Library, fibrositis is unlisted as such in two of them; in the other volume (Volume 5, Third Series) there are only fourteen articles on the subject. Appearing between 1912 and 1922, all but two of these reports came from England. In the thirty volumes of the Quarterly Cumulative Index and the Quarterly Cumulative Index Medicus (1916-1935) only two articles are listed under the term "fibrositis," none since 1920. Thereafter the indices give: "Fibrositis, see Myositis or Rheumatism." Under "myositis," however, are articles on Bornholm's disease, tropical myositis, gonorrheal and syphilitic myositis, myositis ossificans, and progressive myositis fibrosa. None of these concern the disease which Dr. Slocumb is discussing. A few articles on fibrositis are to be found under the heading "rheumatism," a term which in England means chiefly acute rheumatic fever, but which in this country means either nothing or almost anything. I mention this to show how insecure a place the term "fibrositis" has in American medical literature.

What then is "fibrositis," a new disease or a new name for an old disease? The term was introduced in 1904 by Gowers and by Stockman to indicate an inflammatory hyperplasia of white fibrous tissue anywhere in the body. It is a useful and relatively accurate term; one justified by the basic pathology of the disease. The several anatomic forms of this disease have been wandering around, separate and unclaimed, hunting for their common parent. Some of these anatomic forms have long been called, by Osler and others, "indurative headaches," "cephalalgia," "capsular rheumatism," or "pleurodynia." A newer term is Albee's myofasciitis, which condition so commonly affects the lumbar and lumbosacral areas. The intramuscular form is the layman's "muscular rheumatism," the general practitioner's "myositis." But these are poor terms and less accurate than "fibrositis" because the disease does not primarily affect muscle cells themselves but is an interstitial, not a parenchymatous, disease of muscles. The obvious outward evidence of this is the lack of significant muscle atrophy in primary fibrositis (a feature which contrasts sharply with the muscle atrophy that accompanies the secondary fibrositis of atrophic arthritis).

At first the clinical features of periarticular fibrositis (the jelling phenomenon, pain in stretching the capsule, the seasonable and weather effects, the vagrancy and variability in the pain, and other features which Dr. Slocumb has mentioned) may seem vague and indefinite, but careful attention to the oft-repeated story will show the features to be quite consistent

and sufficiently distinctive that the disease can usually be readily differentiated from "arthritis," which the overly sympathetic or uninitiated call it, and from "nervous exhaustion," which the unsympathetic are likely to call it. Varying degrees of chronic nervous exhaustion and fatigue are practically always present, but the exhaustion is part of the disease, a symptom of fibrositis just as another type of chronic nervous exhaustion is a symptom of hyperthyroidism.

The patient with periarticular fibrositis at first usually gets little sympathy. He may complain petulantly, even bitterly; but he looks well, his physical examination, laboratory tests and roentgenograms are generally quite normal, and his joints are undeformed and freely movable. It is then that his condition is likely to be called just "neuromuscular pain" or "psychalgia." When the complaints continue, the physician may give the patient the benefit of the doubt and, suspecting early "arthritis," tag the patient with such a diagnosis, thus initiating even greater worries and phobias. Thereafter these anxious unhappy patients continue on their aching but undeformed way, almost more annoyed than pleased that the "deforming arthritis" which they so fully anticipate forever seems to be postponed. If the expected deformities would only appear, if they could "only get it over with," they would be almost more satisfied than to have this "sword of Damocles" forever hanging over their heads. But it is this persistent negativity of their examination that should convince us that arthritis cannot be present. This negativity is relative, however, for there may be some periarticular thickening, and in about 50 per cent of the cases, definite subcutaneous nodules are palpable most commonly in the region of the sacroiliacs or iliac crest. From our own studies and those of Stockman we are fairly familiar with the pathology of the nodules. When nodules are absent, some believe the diffuse muscular pains to be a neuralgia of sensory nerves of muscles. Thus, the weakness of our presentation and that of others is the meager data we have on the pathology of the disease as it affects muscles, but particularly joints. This we are trying to remedy and our studies on pathology to date seem to give us histologic evidence that a true arthritis is not present in periarticular fibrositis and that the integrity of interarticular tissues is indeed maintained.

DR. JAMES R. TILLOTSON, LIMA, O.—What relation has occupation to this condition?

DR. WILLIAM J. KERR, SAN FRANCISCO, CALIF.—We have in the hospital at the present time a male patient, thirty-two years of age, who for ten years has had some rigidity of the spine, and in recent weeks some involvement of the muscles of the face, arms, thighs, and calves. When one examines the lower extremities in the region of the gastrocnemius muscle, he may find rather elongated areas that are somewhat firm. The patient can find them more rapidly than the physician at first. In one instance the firm area was about four inches in length and one-half inch in thickness. In attempting to secure a biopsy of this nodule in the gastrocnemius muscle, we had a great deal of difficulty. We thought it was just beneath the external surface of the muscle, but we had to go very deep to get any tissue that seemed to be abnormal in appearance. This tissue showed the same characteristics as have been mentioned here. I do not know exactly how many nodules were found, but I believe five or six. In Great Britain it seems to be the practice among some physicians to forcibly break up these nodules. Our patient is still under treatment, and we shall report on him later.

DR. M. HENRY DAWSON, NEW YORK, N. Y.—The nodules in fibrositis are painful, while the nodules in rheumatoid arthritis are rarely if ever painful. We are of the opinion that the histologic structure of the rheumatoid nodules is quite distinctive.

DR. RUSSELL L. CECIL, NEW YORK, N. Y.—As Dr. Hench says, this disease we speak of as fibrositis is very much in need of a more substantial pathologic background. Take the condition so commonly known as acute lumbago, which very often follows a strain or some unusual movement; we know that some of these attacks are caused by wrenching a joint which is already affected by arthritic changes, as shown in the x-ray. We know there are other instances where congenital anomalies of the spine produce the same sort of attacks. Then there is a condition often spoken of as myositis or fibrositis where the x-ray failed to reveal any change in the back except some defect in posture. In our experience a great many of these

posture cases are very quickly cured and relieved of future attacks by improving the posture. All orthopedic men are familiar with this type of case. I wonder how many of these cases should be spoken of as "fibrositis." I wonder whether most cases of myositis or fibrositis of the lumbar region cannot be classified as mechanical maladjustments of weak backs due to the posture of the patient.

Question: I would like to ask whether you find endocrine imbalance, especially ovarian or thyroid, in cases of fibrositis.

DR. CHARLES H. SLOCUMB, ROCHESTER, MINN. (closing).—Regarding occupation, in England, as you will notice in that chart reproduced from Buxton, 55 per cent had fibrositis. The people that came to Buxton were miners and workers in factories where they got cold and damp. I believe from those figures that patients with fibrositis are definitely made worse in cold, damp places.

The reference to the breaking up of the nodules is a very good one. Stockman and others use a firmer massage for patients with fibrositis than for patients with arthritis.

Dr. Dawson commented about the nodules. The nodules in infectious arthritis and fibrositis are practically the same. Many of the nodules in fibrositis are not tender.

In connection with Dr. Cecil's question regarding whether or not attacks of lumbago and muscle soreness are actually myositis or fibrositis, I cannot answer. There is a need for considerably more pathologic work in some of these cases. However, there is a large group that clinically and pathologically are fibrositis rather than myositis or arthritis.

As far as the effect of endocrines is concerned, I cannot link definitely any endocrine deficiency with primary fibrosis. There are several men who feel that deficient thyroid is a factor. However, they feel it may not be a specific factor. People with deficient thyroid usually become overweight and obese and have considerably more subcutaneous tissue than normal. If a patient has panniculitis, the symptoms are much worse proportionately with the amount of subcutaneous tissue present. Treatment with thyroid in the overweight group seems to give them additional help, more especially with the weight loss than a specific effect of the endocrines themselves.

DIFFERENTIAL DIAGNOSTIC POINTS OF CONSTITUTIONAL CONDITIONS MISTAKEN FOR ARTHRITIS WHICH PRODUCE SKELETAL ACHES AND PAINS (ARTHRALGIAS, NEURITIS, RHEUMATISM)*

WILLIAM J. KERR, M.D., SAN FRANCISCO, CALIF.

IN CONCLUDING our presentation of the diagnostic criteria of diseases of the joints, I shall mention some of the less common conditions which may be mistaken for the diseases previously discussed.

The terms rheumatism and neuritis are used loosely by the public to denote almost any conceivable type of pain. To determine the origin of the symptoms, the clinician needs a comprehensive knowledge of medicine.

Syphilis.—Arthritis occurs in the early and late stages as well as in congenital syphilis. As a rule the lesions are bilateral, of long duration, and not especially painful. In congenital syphilis, dactylitis with fusiform swellings of the fingers and rarely of the toes is common. A chronic bursitis and myositis of the calf and sternomastoid muscles are occasionally observed. Periostitis is a common complication in acquired and congenital syphilis, late in the first decade. Meningeal involvement may cause generalized aches and pains. In late syphilis, lesions in the central nervous system and sensory roots are responsible for peripheral pain, crises in the viscera, and destruction of joints of the Charcot type. Syphilitic spondylitis is not rare. Deformities of the spine due to a destructive syphilitic process may cause severe radicular symptoms.

The history, the general search for other syphilitic lesions, the serologic tests and the x-ray examination will usually establish the diagnosis.

Hemophilia.—Hemarthrosis, due to bleeding from the synovial membrane, is not uncommon. As a result, arthritis and deformity may occur. The larger joints such as the elbow or knee are more often involved. The patient is a male, usually in the years before puberty, and there is a history of being a "bleeder" from infancy. Other male members of the family have been affected. The clotting time on the blood is prolonged greatly and the platelets are normal in number. The bleeding time is normal, and the clot retracts normally.

Scurvy.—The changes in and about the joints in scurvy are not specific but are sites for hemorrhage as a part of a general tendency to bleed. In marked cases the periosteum near the joint will be elevated from the ends of the bone and can be demonstrated by the x-ray. The tendency to bleed is apparently due to a loss of the intercement substance joining the endothelial cells of vessels. Hemorrhages may be observed generally, and the gums are usually spongy. There is a variable anemia. Tests for capillary resistance by the exhibition of

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negative pressure show a greater tendency to purpura than the normal control. Patients with active rheumatic fever have been considered as sufferers from deficiency of vitamin C by some workers on the basis of this test. The remarkable effects following the administration of vitamin C will support the diagnosis of scurvy.

Beriberi.—The dry or polyneuritic form of beriberi, due to deficiency of the antineuritic vitamin, may cause confusion in diagnosis if not kept in mind in patients with pains and weakness in the extremities. Paresthesias, impaired sensations, and weakness and tenderness of the muscles may be observed. In the wet type with edema, the nutritional disturbances from lack of proteins in the diet may mask the general wasting. A history of probable dietary deficiency and the response to treatment are helpful in establishing the diagnosis. The cardiac complications may be striking.

Rickets.—A disease of childhood characterized by wasting of the muscles, pallor, and swellings in the ends of bones at the epiphyseal line and showing characteristic nodular areas at the costochondral junction (the rickety rosary). The entire skeleton participates in the loss of calcium from the bones. The general examination will usually establish the diagnosis of rickets except in the early stages and the x-ray films will show the irregularity of development at the epiphyseal line. The use of large doses of irradiated ergosterol in the treatment of chronic arthritis is dangerous. I have recently had a patient who was first seen after taking 2,300,000 international units per day for eighteen days. After fifteen days he suffered from thirst, polyuria, and weakness and then passed into coma ending in death. This is, I think, the first known death from acute fatal poisoning with vitamin D in man.

Raynaud's Syndrome, Scleroderma and *Arthritis* are frequently associated in advanced cases. It is not entirely clear what the relationship is, but it is likely that the vascular disturbances in Raynaud's syndrome lead to faulty circulation of the joints and the skin. The condition of scleroderma, especially of the fingers, involves the deeper tissues diffusely and the long-continued constricting influence of the aging scar-tissues tends to impede progressively the flow of blood to the digits. I have seen scarcely a patient with advanced symptoms of Raynaud's syndrome who did not present thickened skin and swollen joints of the fingers in addition to the changes in color brought on by cooling. The fingers are frequently slightly flexed. The extent of necrosis of the tips of the fingers is variable, but x-ray films generally show demineralization of the phalangeal bones and acral destruction resembling the changes seen in leprosy.

Leprosy.—Paresthesias associated with impaired sensations in the extremities may be seen in leprosy. The loss of tissue in the digits may be extreme in late cases, but early when the mixed nerves are irritated by the localized process in them, the symptoms may resemble closely those described in Raynaud's syndrome and scleroderma. An examination of the mixed nerves to the extremity for enlargements and a biopsy may be diagnostic or other lesions may be found in the skin or nasal mucous membranes.

Cervical Rib and the *Scalenus Anticus Syndrome* occasionally cause disturbances in circulation to the hand and fingers on one or both sides or may

cause symptoms of radiculitis. In some cases the local signs in the fingers may be very striking with changes in color, swelling of interphalangeal joints and necrosis of the ends of the digits. Careful examination for cervical ribs, and configuration of the upper thoracic and cervical regions will help in the diagnosis. A long neck with "Champagne shoulders" will suggest the scalenus anticus syndrome. The onset of symptoms in middle life with a gain in weight, stooping of the shoulders and the development of pulmonary emphysema contribute to the onset of symptoms. In a number of patients coming under observation in recent years, an arthritis or scoliosis in the lower cervical spine apparently was the cause for striking peripheral changes in the hands and fingers, probably through the effects on the nerve-roots.

Erythralgia, formerly called erythromelalgia, observed in the extremities is characterized by pain and burning sensations, discolorations and swelling, and a feeling of warmth. The arteries may pulsate markedly. Stasis plays a major part in the causation of the burning pain. A disease of the joints may be suspected but the involvement of the joints is secondary to vascular and nervous disorders. Fixation from disuse and contractures are late results.

Peripheral Neuritis is most frequently associated with alcoholism but may be observed in a number of so-called toxic conditions. Patients with chronic arsenical poisoning may develop painful joints in the extremities resembling rheumatoid arthritis. Some patients who are candidates for typical rheumatoid arthritis will come for relief of symptoms consistent with peripheral neuritis or myositis or they may show vascular symptoms suggesting Raynaud's syndrome weeks before the full clinical picture is apparent. Primary anemia and diabetes are common examples of constitutional diseases causing sensory or motor symptoms in the extremities. Myositis on the basis of such inflammatory lesions as are seen in trichinosis and dermatomyositis are often mistaken for some type of arthritis. The cramplike pains of intermittent claudication; pains in the lower extremity resulting from falling arches; and pains of Paget's disease are also confused with symptoms of arthritis. Periarteritis nodosa in the more acute form may show swelling and pains in the joints. The associated symptoms of fever and localized tender nodules along the arteries may help establish the diagnosis which would be confirmed by microscopic sections of the arteries involved. The close association of this disease with the arteritis of rheumatic fever is apparent. The differential diagnosis between many of the disorders just mentioned may be very easily made following a careful history and complete examination but in some cases of neuritis and myositis no etiologic factor may be found. In recent years we have seen a number of young subjects with extensive peripheral neuritis following upper respiratory symptoms, with fever and irritation of the meninges. Whether this is an atypical form of poliomyelitis or some other obscure infection is difficult to determine. Fibrositis is commonly described abroad, but we seldom make the diagnosis in this country. We have just seen a patient, male aged thirty-two, in our clinic who presented transient tender nodules in the subcutaneous tissues and muscles. The histologic picture was one of infiltration with cells of different types. There had been rigidity of the spine for several years.

This brief résumé of some of the conditions which may cause the patient to seek aid for supposed arthritis or "rheumatism" omits discussion of many. A few of these will be mentioned in closing: Osteomyelitis, herpes zoster, von Recklinghausen's diseases of bones and nerves, psychogenic pain, referred visceral pain, e.g., cardiac pain and many others. Pain and swelling in weight-bearing joints incident to a sudden gain in weight have been mentioned in a consideration of other types of chronic arthritis.

DISCUSSION

DR. JOHN H. MUSSER, NEW ORLEANS, LA.—There are several conditions which are quite frequently associated with pains in the joints. The first of these is anemia. The pains may be due, not to the deficiency in vitamin diet to which Dr. Kerr referred, but to the anemia. The pain in the joints is quite common without any roentgenologic evidence of arthritis. Stiff and painful shoulder for which there were some sixteen causes, is a condition in which it is hard to make an etiologic diagnosis. In a child who develops arthritis following an injection of serum, in the first twenty-four hours it becomes quite a problem to determine whether that joint is the result of the injection of serum some seven to ten days previously or whether it is part of the complications of, say the associated meningitis. Last, I was told some years ago by a physician patient of mine that it was very common for him, when he was having attacks of angina, to develop pain in his left elbow. He noted that very frequently after some slight exertion this pain would develop in his left elbow, and yet he would not be conscious of any substernal distress or pain down the arm. Since that time I have noted quite a few people with angina whose referred pain confined itself to the elbow. I was particularly fortunate some time ago in having a man who complained of pain in his left elbow after he had taken exercise. An electrocardiogram was made and the curve was that associated with coronary disease. On treatment of the coronary disease the pain in the elbow disappeared.

As Dr. Kerr has indicated, there are many conditions which may be responsible for so-called arthritis or rheumatic aches and pains throughout the body. I think that the important lesson he points out to us is, that we must not be satisfied to diagnose arthritis without a thorough survey of the patient.

LABORATORY METHODS

THERMOCOUPLES FOR THE MEDICAL LABORATORY*

Guiding Principles and Methods of Constructing Apparatus for Surface, Cavity, and Intramural Thermometry

Paul C. Foster, Ph.D., New Orleans, La.

THE thermocouple, discovered over a century ago, has found an increasing usefulness in clinical and physiologic investigation. Unlike mercurial thermometers, thermocouples quickly come to thermal equilibrium with their surroundings, making rapid temperature determinations possible Their mass may be made small enough that they produce negligible temperature changes in the medium into which they are introduced. Not only may surface temperatures be determined but, by placing the junctions in appropriate hypodermic needles, catheters, cannulas, etc., it is possible to determine temperatures in the muscles, liver, brain, and other solid viscera, in veins and arteries, in the stomach, rectum, bladder, kidney, and other hollow viscera.

GENERAL PRINCIPLES

The principle of the thermocouple is too well known to deserve much discussion. Seebeck first observed that in a circuit composed of two different metals a current of electricity flowed when one of the junctions between these metals was hotter than the other. The direction and amount of current depends on the kinds of metal and the temperature of the junctions. For example, in a copper-iron circuit one junction of which is 0° C. and the other 100° C., current flows from copper to iron across the hot junction and from iron to copper across the cold. The opposite to the Seebeck effect was observed by Peltier, who noted that electricity flowing through a circuit of dissimilar metals gives off heat at one junction and absorbs it at the other. The thermocouple is thus a reversible heat engine, although a very inefficient one. In thermoelectric circuits there are electromotive forces not only at the junctions, but also, as Lord Kelvin showed, in the homogeneous conductors between the junctions, as they are not at the same temperature throughout. Only the Seebeck effect concerns us here.

Although any two dissimilar metals may be used for thermocouples, only those giving high relative thermoelectric power and obtainable of standard composition and in convenient wires are chosen. The popular ones are iron or constantan with silver, copper, or manganin. Constantan, while not giv-

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ing as high relative thermoelectric power as iron with the above metals, has the advantage of being noncorrosive, and in combination with copper gives the best thermocouples for medical use. Bismuth-antimony couples have the greatest thermoelectric power of any combination but are used only in radiometers. Iron and constantan are often used together because their curves are about parallel on the thermoelectric diagram, hence the relation between temperature difference at the junctions and the EMF generated is practically linear. But with any of the other usual combinations of metals the relationship between temperature and EMF is also a linear one at the temperatures required for medical work. Introduction of a third metal into a thermocouple circuit does not matter, provided both junctions of this conductor are at the same temperature. When two or more thermocouples are connected in series, the combination is called a thermopile, which, when designed and calibrated to receive and measure radiant energy, is spoken of as a radiometer.

Although descriptions of many excellent pieces of apparatus have been published, some are needlessly complex and the details of construction are often not available. In this paper an apparatus is described in such detail that any technician can construct it. Several such instruments have functioned perfectly for two years in our own and other laboratories and have proved to be sturdy, reliable, and easy to operate.

Designing a thermocouple depends on the use which is to be made of the instrument. Portability, for example, is gained at the expense of sensitivity. Such an instrument as designed by Scott[1] and now familiar as the Tycos dermatherm, while possessing portability and simplicity, does not have great sensitivity, and, because it consists of a number of thermocouples arranged in series (a thermopile) and mounted in an applicator having considerable heat capacity, is not absolutely accurate. Furthermore, the readings are subject to considerable variation, depending on the technic with which the electrodes are applied. Where temperatures are to be taken intramurally or within cavities or solid viscera construction of thermopiles small enough to fit hypodermic needles or small catheters is virtually impossible. For all work where such intramural or cavity temperatures are to be taken simultaneously with surface temperature, it is better to use single thermal junctions and substitute a more sensitive although less portable galvanometer. Portability is a consideration often exaggerated. In most cases it is as easy to bring the patient to the thermocouple as to carry the thermocouple to the patient. The apparatus can be permanently set up in a laboratory or operating room, but it is no great difficulty to move it if necessary.

The essential parts of a thermocouple for medical work are: (1) the exploring junction which is fitted to an applicator of appropriate design for exploration of the desired structure, (2) the reference or constant temperature junction, and (3) the galvanometer or other current measuring device.

EXPLORING JUNCTIONS

Surface Thermocouples.—Absolute accuracy in obtaining surface temperatures is difficult to achieve. Junctions which are included in applicators of appreciable mass are objectionable since when applied to the skin they with-

draw heat and falsely low temperatures are recorded. If they are left in contact with the skin long enough to reach equilibrium, they prevent the normal loss of heat by radiation and falsely high values result. This is the principal objection to instruments such as that of Scott.[1] Such instruments during use tend to become warm and the temperatures recorded gradually rise, this being especially noticeable when a cold area is studied immediately after a warm one. It is almost impossible for two observers to obtain values which check, since the amount of pressure with which the applicator is applied and the length of time it is held in place so greatly influence the readings. These are well-known objections to the use of surface thermometers and have led many experimenters to entirely discontinue their use. The use of uncovered junctions is free from the objection that normal heat loss from the skin is prevented, but here another objection arises. With bare skin surface of one temperature and air of another, the temperature recorded by the thermocouple tends to be a middle value. It is clear from observations that the smaller the diameter of the wire used in the junctions the less this objection becomes. With small wires the mass and therefore the heat capacity is cut down and equilibrium is quickly reached. Small wires are also less influenced by the air temperature about them. Since the thermal conductivity and heat capacity of tissue are very high in comparison with that of air, the temperature assumed by the wire must be much more nearly that of the tissue than that of air. Moreover, the air adjacent the body approaches the temperature of the skin. We have not observed that the degree of pressure with which bare wire junctions are applied influences the values obtained provided the pressure is sufficient to make a firm contact. We have been entirely unsuccessful in designing supporting applicators for the junctions which gave satisfactory results when the applicator came in contact with the skin areas being studied, and for that reason use uncovered junctions of No. 40 wire where we desire great accuracy. These being necessarily fragile a No. 35 wire is used with good results for most routine work. These are held in place with silk thread when it is desired to have them on the skin for long observations. Where it is desired to make single examinations of numerous skin areas a junction stretched between the prongs of a wishbone-shaped wooden fork is used. It is absolutely necessary to protect the junctions from the electrolytic action of sweat by the use of shellac or insulating varnish. Junctions should be made with the smallest amount of solder consistent with the formation of a good union.

The use of the thermocouple method in determining skin temperature has been criticized by Hardy[2] on the ground that such instruments give readings which are too low as compared with those taken indirectly by radiometric methods. The instruments compared by Hardy, however, all have a high heat capacity. Hardy[3] describes a radiometer, which is similar to that used by Cobet and Bramigk.[4] No doubt the radiometric method is theoretically the correct one for skin temperature measurement, but anyone who has worked with radiometers knows the difficulty of constructing and using them for any but the most exacting purposes. A further objection to Hardy's instrument is that it is not adaptable for determining the temperature of small areas, for example, a single digit.

Hypodermic Thermocouples.—Hypodermic thermocouples have been used by many observers, notably Bazett and McGlone,[5] Sheard,[6] Clark.[7] After considerable experience with such needles we are convinced that the one described here is reliable, and its construction simple enough for technicians of modest ability. The needle holder consists of a hub and cover turned from bakelite rods according to the dimensions shown in Fig. 1. The hub is drilled with a No. 72 twist drill and a groove filed on one side of its shaft as shown. The needle of No. 26 gauge stainless steel tubing* is cut to the desired length by nicking sharply with a safety razor blade, breaking in the same manner as with glass tubing, and honing one end to a beveled edge The thermal element consists of No. 42 gauge enameled constantan† and copper wires. Six-inch lengths of these wires are passed through the needle and allowed to project from the beveled end. The wires are scraped free of enamel for a distance of about 1 mm., these bare areas placed in apposition and drawn back until they are at the point of the needle. Noncorrosive soldering flux is applied to the wire and needle and holding the needle tip and wires within a drop of melted solder the wires are drawn into the needle until the bare portion just disappears within the bevel. The needle is removed from the hot solder and by traction it is determined whether the wires are securely soldered in place. The lumen of the needle should be completely occluded, applying a little flux and reintroducing into the melted solder if necessary. Excess solder and any projecting wires are shaved off the bevel or sides of the needle with a safety razor blade.

The wires and blunt end of the needle are passed into the hub of the needle holder and a little bakelite cement worked in around them. Several turns of silk thread secure the wires to the shaft of the hub. Flexible leads (described later) are also tied to the shaft and the corresponding lead and needle wires soldered together. The whole shaft is given a thorough wrapping of silk thread and a coat of shellac.

Before use, the needle should be tested to make certain that the thermal junction is at the point. Occasionally during construction the enamel on the wires is broken, resulting in the true junction being elsewhere than in the tip, this occurring most frequently at the end where the wires emerge from the needle. When immersed in warm water to a depth of 3 or 4 mm. the needles should give practically the same galvanometric deflection as when totally immersed. Needles may also be tested by holding the entire length in the mouth against the tongue and slowly withdrawing. The galvanometer should show the same deflection until the last 3 or 4 mm. pass through the lips. Particularly the region at the base of the needle should be tested to make certain that warming with the fingers does not produce a deflection of the galvanometer.

These needles are so designed that the tube is not part of the thermocouple which obviates the necessity of having lead wires and tubing of the same material. The external diameter of these needles is 0.44 mm. and a 3.5 cm. needle complete with wires soldered in place weighs only 35 mg. It is

*Obtainable from Becton, Dickenson & Company and sold under the trade name "Erusto."

†Constantan is manufactured by Driver-Harris Company, Harrison, N. J., and sold under the name "Advance Wire." They can furnish all sizes with enamel, cotton, or silk insulation.

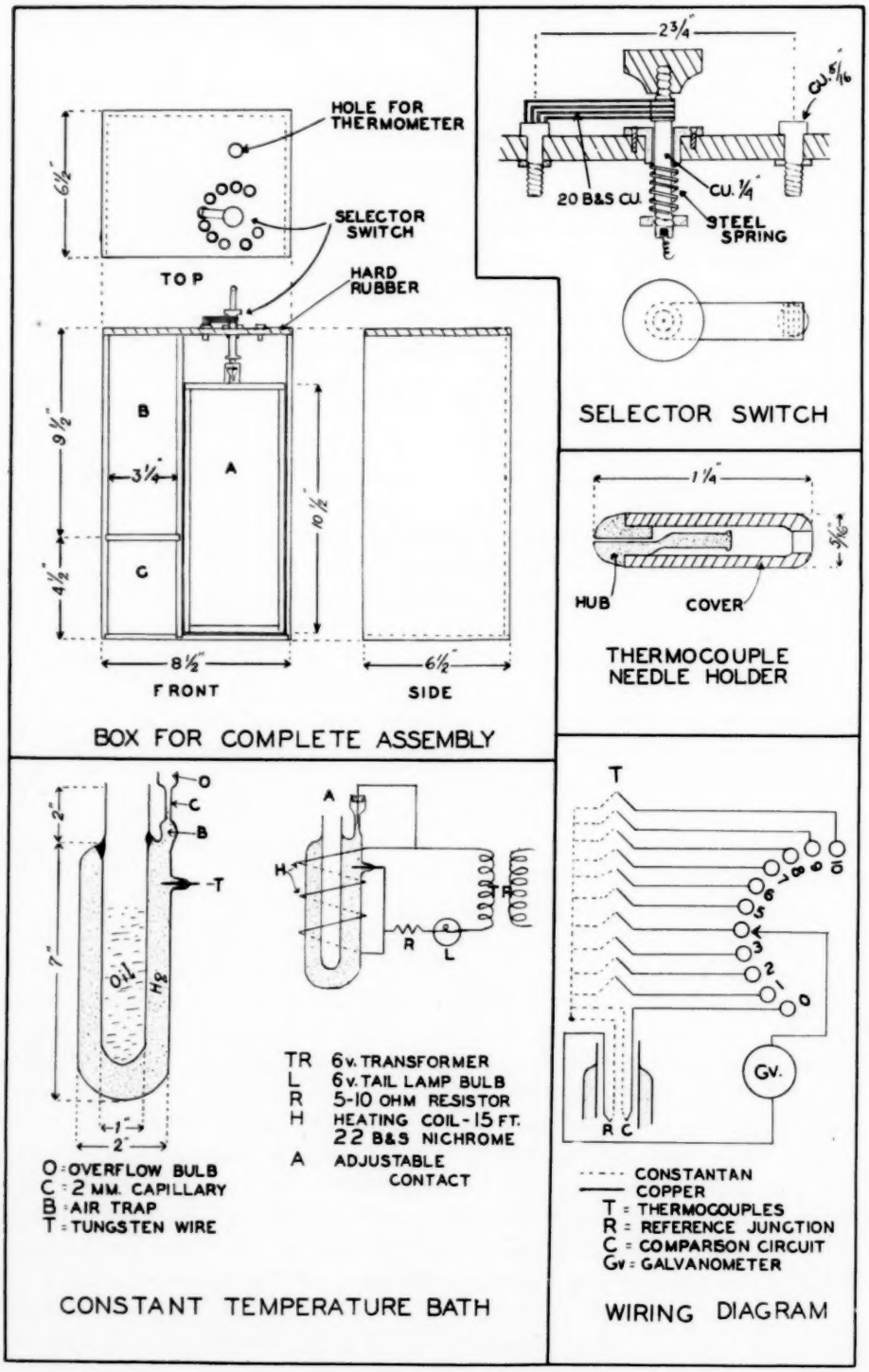

HOLE FOR THERMOMETER
SELECTOR SWITCH
TOP
HARD RUBBER
B
A
C
3¼"
9½"
4½"
10½"
8½"
6½"
FRONT
SIDE
BOX FOR COMPLETE ASSEMBLY
2¾"
CU. 5/16"
20 B&S CU.
CU. ¼"
STEEL SPRING
SELECTOR SWITCH
1¼"
5/16"
HUB
COVER
THERMOCOUPLE NEEDLE HOLDER
O
C
B
T
2"
7"
1"
2"
Oil
Hg
O = OVERFLOW BULB
C = 2 MM. CAPILLARY
B = AIR TRAP
T = TUNGSTEN WIRE
A
H
R
L
TR 6v. TRANSFORMER
L 6v. TAIL LAMP BULB
R 5-10 OHM RESISTOR
H HEATING COIL - 15 FT. 22 B&S NICHROME
A ADJUSTABLE CONTACT
CONSTANT TEMPERATURE BATH
T
10
9
8
6
5
3
2
1
0
Gv.
R C
CONSTANTAN
COPPER
T = THERMOCOUPLES
R = REFERENCE JUNCTION
C = COMPARISON CIRCUIT
Gv = GALVANOMETER
WIRING DIAGRAM

Fig. 1.

not difficult to make smaller needles if desired. The "Erusto" described here is the smallest obtainable, although tubing of other metals can be obtained in smaller sizes.

The use of hypodermic thermocouples is open to certain theoretical objections. There is obviously heat transfer along the metal which may alter the temperature of the tissue in the vicinity of the junction. The smaller the diameter and, therefore, the less the mass of the needle the smaller this error becomes. Bazett and McGlone[5] have written at length regarding this error and have derived a formula for making corrections. They made use of agar plates in which a thermal gradient was created, making temperature observations at various depths with two needles, one of which was placed transversely (and therefore essentially isothermic throughout its length), the other placed vertically. Experiments carried out by us on agar plates point to a similar systematic error in the readings of needles placed vertically through jelly having a temperature gradient. This largely disappeared when the needles instead of being introduced vertically to a given depth were introduced obliquely. With needles 5 cm. long introduced obliquely to their full length the error was negligible until vertical depths of greater than 1 cm. were reached. Experiments on the living subject, where the temperature gradient of the subcutaneous tissue was reversed by warming the skin, indicated that heat transfer along the needle must play a negligible rôle. One such experiment is given in Fig. 2. Thirty minutes after introduction of the needles into the anterior aspect of the thigh the temperatures at various depths were as shown in the figure. On irradiating the skin with a powerful source of infra-red the surface temperature began to rise instantly, followed fifteen seconds later by the temperature at a depth of 2 mm. and forty seconds later by that at 7 mm., but the temperature at 15 mm. did not begin to rise for one minute although by this time the needle was passing through skin which had reached a temperature of 39° C. If any considerable amount of heat were being transferred along the needle, this temperature would have gone up sooner. Examining the curves at the time when the infra-red irradiation was discontinued, it is noted that the surface temperature falls instantly, followed about fifteen seconds later by the temperature at 2 mm., a little later by that at 7 mm., but there was actually a continued rise in temperature at the 15 mm. depth, even though the surface and more superficial tissue already were cooling rapidly. If any considerable amount of heat were being transferred along the needle from the heated surface, the temperature should start falling as soon as the irradiation was stopped. The relation of the temperature curves at these depths is such as would be expected on the basis of heat being transferred slowly through tissue which has a high specific heat and low conductivity, and by the relatively slow transfer due to blood flow. The experiment cited here is only one of many scores. In other experiments sponges saturated with alcohol were placed over the exposed parts of the needle during the irradiation without affecting the temperature readings at the depths. One reason for the apparent lack of influence due to heat transfer in the needle

may be that the thermal element being independent of the wall of the needle and somewhat heat insulated by the enamel is protected partially from the gradient in the needle itself.

The vertical depth of the point of an obliquely placed needle may be estimated by noting the angle of the needle with the skin and the distance to which it was inserted, and then duplicating these conditions on coordinate paper. The accuracy was tested on agar plates, inserting the needles, withdrawing them and estimating their depth, then checking the results by cutting away the agar and actually measuring the depth to which the needle had penetrated. Roentgenograms also showed that on human subjects the estimated depth was usually correct within 1 or 2 mm.

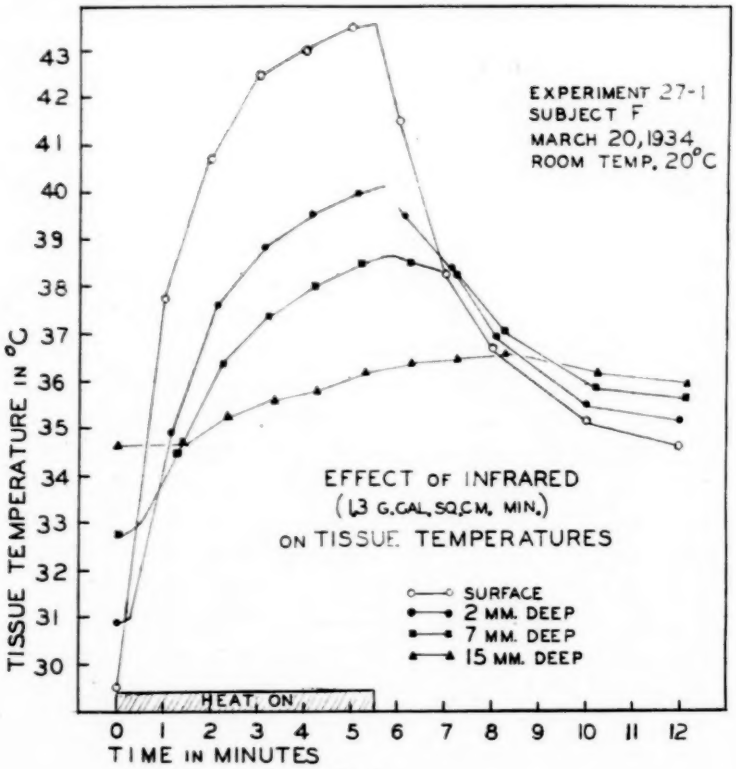


Fig. 2.

Sheard[6] has described a variety of thermal junctions placed in various forms of catheters for use in determining gastric, rectal, and other cavity temperatures. Huggins[8] placed junctions in ureteral catheters and determined the temperatures in the urinary tract as far as the kidney pelvis.

CONSTANT TEMPERATURE JUNCTION

The constant temperature junction may be placed simply in a thermos flask with water, air, or oil of any known temperature. Ice is to be avoided since the resulting currents are too large to be handled by the galvanometer without great sacrifice in sensitivity. About the middle of the range being determined is the best temperature at which to maintain the constant temperature bath.

A self-regulating temperature bath for the reference junction is well worth the trouble of construction for convenience and for accurate work. Ours, Fig. 1, modified after Clark[7] and Sheard,[6] consists of a double-walled Pyrex flask, the outer compartment of which is filled with mercury and electrically heated. The mercury on expanding rises in the capillary and closes the shunt circuit through the mercury, thus short-circuiting out the heating coils. The small bulb, *B*, is essential, otherwise when the mercury contracts on allowing the thermostat to cool, air may get into the flask and being trapped there cause the thermostat to operate at a new level on reheating. About three kilos of mercury are required to fill the flask. The thermostat is filled with a funnel and fine capillary keeping the mercury level well up in the funnel to keep oxides from entering the flask. The mercury level varies about 2 mm. in the capillary with each 0.1° C. variation, thus permitting accurate adjustment. The inner tube containing the reference junction is filled with mineral oil, which must be of excellent quality to avoid corrosion.

The heating element consisting of 15 feet of No. 22 nichrome wire having a resistance of about 15 ohms, is coiled around the bare flask and held in place with a few layers of plaster-of-Paris bandage. A 6 v. toy or bell ringing transformer with an output of about 25 watts heats the coil. To protect the transformer secondary when the current is flowing through the low resistance mercury shunt a 6 v. automobile tail light bulb is placed in series, this bulb also serving as a pilot lamp, burning bright when current is flowing through the mercury and dim when the apparatus is heating. Some transformers have a little more than the rated output and burn out the bulbs rapidly, in which case an additional 5 or 10 ohms of resistance to cut down the voltage is the remedy. Bulbs allowed to burn only at dull to bright red last indefinitely.

The thermostat is placed in a box, the top having holes for the glass tubes, and is thoroughly packed with loose asbestos. A nichrome wire thrust through a cork in the overflow bulb is a satisfactory contact. To depress the temperature at which the thermostat operates add mercury to the system; to raise the temperature at which the thermostat operates, remove the shunt contact, allowing the temperature of the flask to rise and remove the mercury which has collected in the overflow bulb. Fine adjustment is made by changing the level of the contact in the capillary.

Thermostats of this design are not entirely free from temperature gradients, but they are small and probably induce a negligible error if the mercurial thermometer and junctions are kept at the same level. Such thermostats are surprisingly stable. One in constant use for twenty months still maintains a steady temperature. Their only disadvantage is that they have to be kept connected constantly with a source of electricity. The temperature, however, does not fall so rapidly, but that they may be disconnected for five to ten minutes for transporting from place to place.

A COMPLETE ASSEMBLY

The complete outfit consists of a self-regulating temperature bath (compartment A in Fig. 1) containing the reference junction which, by means of a selector, can be connected with any of ten junctions. The junctions when

not in use are stored in compartment B. In compartment C is housed the transformer for heating the thermostat, the pilot lamp and protective resistance.

The selector switch, the details of which are shown in Fig. 1, has all its conducting parts made from electrolytic copper. The switch blade has several leaves to insure a low resistance contact. It is entirely free from thermoelectric effects, as proved by the fact that the contacts may be touched with a hot soldering iron without altering the galvanometer deflections. The points numbered 1 to 10 (wiring diagram Fig. 1) are connected with the various thermocouples. The point numbered *0* is connected to a "comparison circuit" and is used for establishing the galvanometer null point.

The leads* may be of any desired length (about 150 cm. is convenient), and each consists of one stranded copper *(Habitual)*† wire and one No. 30 constantan *(Advance)*‡ wire. Leads may be covered with small rubber tubing§ or a neat and sturdy covering for the leads can be made from stranded silk embroidery floss, knotting the thread in half hitches around the wires in much the same manner as a woman "tats." Rather than have many long leads it is more convenient to group three or four pairs of conductors together, separating them into individual leads 25 cm. from their terminations. Such a group is conveniently used for points located near each other as, for example, on one leg.

Each copper conductor is soldered to its corresponding contact on the selector switch as shown in the wiring diagram of Fig. 1. From the rotor of the switch a copper "pigtail" connects with one of the galvanometer leads. The constantan wires are all brought together and soldered to the constantan side of the reference junction. The "comparison circuit" consists of a copper-constantan lead having the same length as the other 10 leads (therefore the same resistance); it is connected with 0 contact and its junction is placed in the temperature bath alongside the common reference junction. Since both these junctions are at the same temperature no current should flow when they are connected with the galvanometer. It is difficult to construct thermocouple circuits entirely free from parasitic currents and such a comparison circuit is useful in setting the galvanometer zero, since it is subject to exactly the same effects as are the other circuits. The copper side of the reference junction connects with the galvanometer. Careful soldering with noncorrosive flux is one of the most important items in thermocouple construction.

CHOICE OF A GALVANOMETER

The choice of a galvanometer depends upon the sensitivity and portability required. For permanent or semipermanent installation a galvanometer of the D'Arsonval type is ideal. Since the resistance of the thermocouple circuit is low, galvanometer coils of low resistance will give the greatest current

*Duplex leads containing one copper and one constantan conductor are obtainable from Leeds and Northrup Company (Philadelphia). These leads are rather inflexible and it is better to construct more flexible ones.

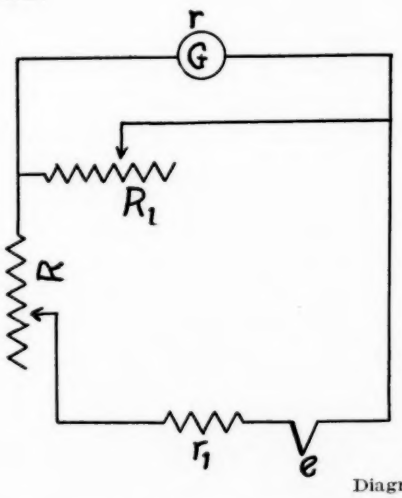
†"Habitual" wire consists of seven strands of No. 35 copper with double silk insulation. Made by Belden Manufacturing Company, Chicago.

‡It would be desirable to have stranded constantan wire but this does not appear to be commercially available.

§Capillary tubing 3 mm. in diameter with a 1 mm. bore is obtainable from the Davol Rubber Company, Providence, R. I.

sensitivity even though their voltage sensitivity is less than with high resistance coils. A copper upper and lower suspension to avoid thermoelectric effects is desirable. The sensitivity of the galvanometer may be diminished by use of heavier upper suspensions, a more stable zero also resulting. Sensitivity may also be diminished by adding resistance to the circuit, but it is of prime importance for rapid work that the system be critically damped. Underdamping (too much external resistance) results in loss of time waiting for the galvanometer to come to rest while overdamping (too little external resistance) results in loss of time through sluggish deflections. For this reason in cutting the sensitivity of the galvanometer, shunt and series resistances should both be used so that the resistance of the shunt in parallel with the thermocouple circuit and series resistance equals the critical damping resistance of the particular galvanometer used. The period of the galvanometer should be as short as possible. The most satisfactory galvanometer tried is a Leeds and Northrup type 2,500 with a 32 ohm coil and copper upper and lower suspensions. Portable galvanometers have not been used but such a one as Leeds and Northrup type 2,400 should be sensitive enough for most work.

Sometimes it is desirable to read accurately a narrow range of temperatures in small divisions, in which case the most sensitive galvanometer suspension possible is required. At other times it may be desirable to read a wider range in larger divisions, in which case a less sensitive galvanometer must be used. In order to use a very sensitive galvanometer suspension not only for narrow ranges of great precision, but large ranges of small precision, and at the same time keep the damping constant, the following circuit was adopted:



e = thermocouple EMF
R = variable series resistance
R_1 = variable shunt resistance
r = resistance of galvanometer
r_1 = resistance of thermocouple

Diagram 1.

Let Ig equal the current flowing through the galvanometer. Then

$$Ig = \frac{e}{r_1 + R + \frac{rR_1}{r + R_1}} \cdot \frac{R_1}{r + R_1},$$

which becomes

$$Ig = \frac{eR_1}{r_1r + R_1r_1 + Rr + RR_1 + rR_1}. \qquad (1)$$

The damping resistance, D, of the circuit, including the galvanometer and its external circuit, is

$$D = r + \frac{R_1 (R + r_1)}{R_1 + (R + r_1)}, \tag{2a}$$

which becomes

$$rR + rr_1 + rR_1 + R_1R + R_1r_1 = D(R + r_1 + R_1). \tag{2b}$$

Substituting the right hand value of equation (2b) for the denominator in (1) we have

$$Ig = \frac{eR_1}{D(R + r_1 + R_1)}. \tag{3}$$

Let a = any sensitivity of the system, then

$$a = \frac{R_1}{R + r_1 + R_1},$$

and

$$R_1 = a\ (R + r_1 + R_1),$$

and

$$R_1\ (1 - a) = a\ (R + r_1). \tag{4}$$

The system will have its maximum sensitivity when R_1 is infinitely large (that is, on open circuit) and will be correctly damped when

$$R + r_1 + r = D.$$

A sample calculation will illustrate the use of these equations. Suppose r = 32, r_1 = 14 and D = 300, then for maximum sensitivity R_1 will be on open circuit and R will be 254. Suppose ½ sensitivity is desired, then from (4)

$$R_1\ (1 - \tfrac{1}{2}) = \tfrac{1}{2}\ (R + r_1),$$

and

$$R_1 = R + r_1,$$

and substituting this value of R_1 in (2a)

$$r + \frac{R_1R_1}{R_1 + R_1} = 300,$$

and

$$R_1 = 2\ (300 - r) = 536;$$

also

$$R = R_1 - r_1 = 522.$$

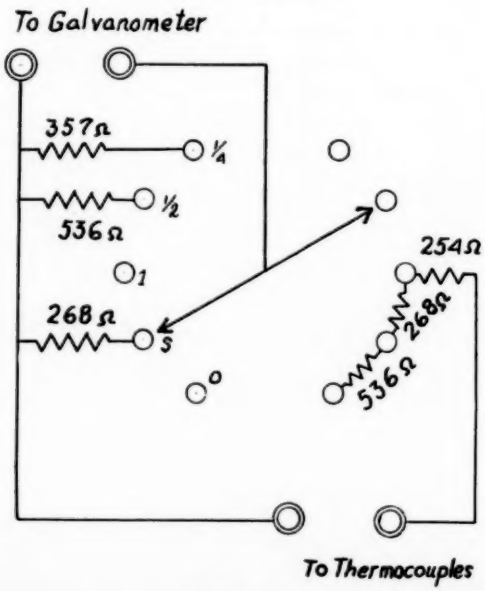


Diagram 2.

The values for R and R_1, with "a" any desired value, are similarly calculated when the resistance of the galvanometer, its critical damping and the resistance of the thermocouple circuit are known. R and R_1 may be two variable resistance boxes, or a shunt can easily be constructed according to Diagram 2.

A change from one range of sensitivity to another is instantly accomplished. Position "O" puts the galvanometer on open circuit and "S" shunts it with its critical damping resistance. These positions, in combination with the zero position on the thermocouple selector switch, are useful in detecting parasitic currents. All conducting parts of the switch should be made of copper and the resistance of manganin. (Manganin has a negligible temperature coefficient of resistivity and a low relative thermoelectric power with copper.)

With the instrument in use in this laboratory 10° C. gives 520 mm. deflection on the full sensitivity range, 20° gives 518 mm. deflection on the ½ and 40° gives 518 mm. on the ¼ sensitivity.

CALIBRATION

Calibration of thermocouples is accomplished by use of water at various temperatures through the range for which the instrument will be used. An axiom, too often not appreciated, is that thermometers read their own temperature, not that of their environment, except when they are in equilibrium. Water at the approximate temperature desired is placed in thermos flasks and thoroughly shaken for five minutes with an accurate mercurial thermometer in place. After reading the temperature the flask is opened and the needle or other junction immersed to its full depth and the galvanometer deflection noted. We always work with the galvanometer null point at the middle of the scale, the reason being that the deflection of a galvanometer is proportional to the current through it only within narrow limits. With most galvanometers the linear relation between current and deflection holds over the range of the full scale when the null point of the galvanometer is at the center of the scale. For this reason the reference junction should be maintained at about the middle of the range of temperature to be determined. With the thermostat described in this paper constancy is possible only when its temperature is maintained above that of the surrounding air.

A series of deflections at various temperatures are plotted on coordinate paper, using the deflection as the abscissa and the temperature above or below that of the reference junction as the ordinate. The resulting curve should be a straight line and should pass exactly through the center of the graph (Fig. 3). With all of the instruments which we have constructed this line, while being straight, passes to one side or the other of the center. We cannot give an adequate explanation but assume that this is due to parasitic currents of small magnitude in the system. The error, however, is compensated for in setting the scale as described later.

The easiest method of constructing a scale is to make the calibration curve on coordinate paper having divisions equal to those on the galvanometer scale (usually mm.). The ordinate representing temperature can be in any arbitrary

divisions. Paper for the scale is laid parallel to the bottom of the graph and, using a "T" square, lines are drawn at exactly the points where the calibration curve crosses the desired ordinates. The scale is numbered arbitrarily in degrees through about the same range that was used in calibration. In use the temperature on the scale which corresponds with the reading of the thermostat is set at the null point of the galvanometer. If the calibration curve did not pass exactly through the center of the graph, compensation is now made. Suppose, for example that, in calibrating, the curve shows that no deflection is obtained when the exploring junction is 0.3° higher than the reference junction, then instead of setting the scale at exactly the same temperature as the thermostat, a temperature 0.3° higher is made to correspond with the null point of the galvanometer. The null point is understood to be

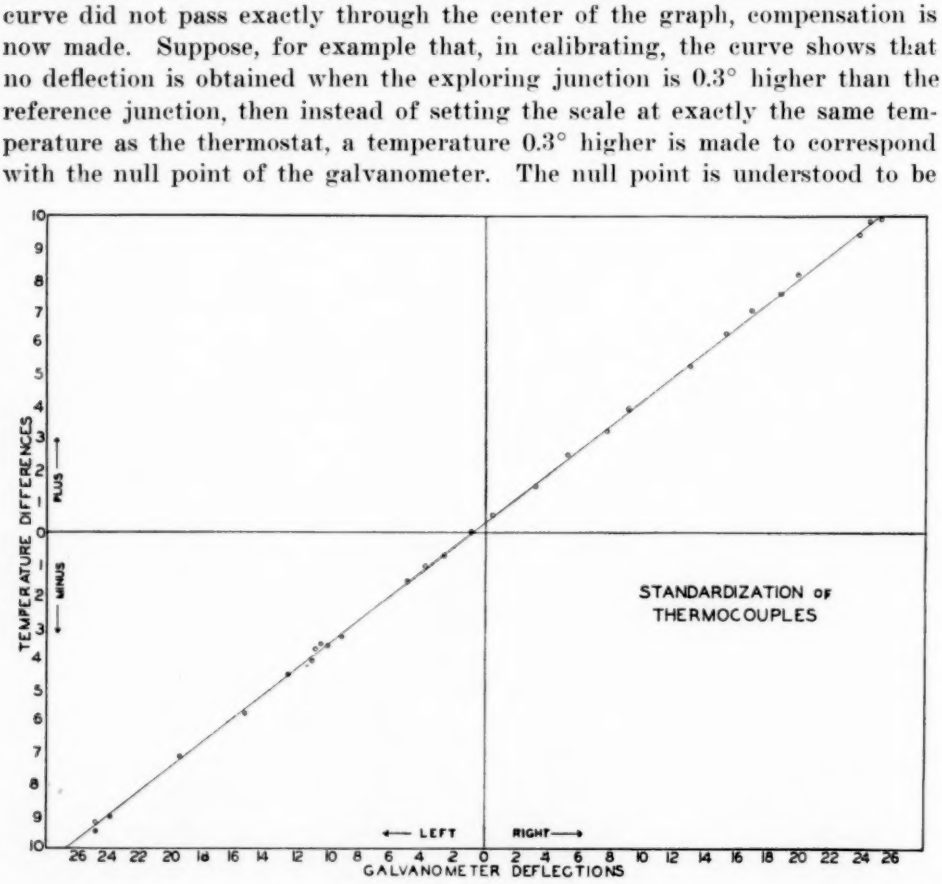


Fig. 3.

that point where the galvanometer comes to rest when the selector switch is on the zero position and both junctions are at the temperature of the thermostat.

It is not necessary to calibrate each exploring junction because when properly constructed they give identical readings. This is checked by placing all junctions in a dry thermos bottle and seeing if they all give the same deflections.

Galvanometers change their sensitivity from day to day, and it is a question as to how often calibration should be repeated. The greatest cause for changes in galvanometer sensitivity is fluctuating room temperature, the galvanometer becoming more sensitive with increasing temperature. Where room temperature does not vary greatly and the galvanometer is left undisturbed,

calibration does not need repetition often. This is especially true where the temperatures being determined do not carry the galvanometer deflections far from the null point. Experience showed that a galvanometer calibrated at 27° C. checked all summer to within 0.1° of the readings of a mercurial thermometer, even when the temperatures being measured were sufficiently high or low to deflect the galvanometer to the limits of a 50 cm. scale, representing 20° C. During this past summer tests were made with room temperatures between 24° and 31° C. Errors of this magnitude can be disregarded in almost all work.

Potentiometric determinations possess the advantage over direct galvanometer readings in that they are not affected by changes in the sensitivity of the galvanometer. Once a potentiometer is calibrated in terms of temperature nothing further is needed as long as the EMF of the standard cell does not change. We have constructed a potentiometer of simple design especially for use with thermocouples, the details of which will appear in a later communication.

SUMMARY

The guiding principles and methods of construction of thermocouple apparatus having a variety of uses in the medical or biologic laboratory for determining surface, cavity or intramural temperatures have been given. Certain pitfalls and criteria regarding the validity of such methods are briefly discussed.

It is a pleasure to express appreciation to Professor D. S. Elliott, Dr. A. B. Cardwell and Mr. C. W. Bosch of the Department of Physics for the use of apparatus and for valuable suggestions; to Professor C. W. Ricker of the Department of Electrical Engineering for suggestions and mathematical solutions; and to Professor Henry Laurens of this department for aid especially in the preparation of this paper.

The apparatus in its present form was made during the summer of 1934 while working at the University of Chicago, and it is a pleasure to thank Dr. C. B. Huggins of the Department of Surgery for his interest and for the services of the technician he so kindly placed at my disposal.

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A RAPID FLOCCULATION METHOD FOR THE DIAGNOSIS OF SYPHILIS*

Technic for Spinal Fluid

F. Rytz, Minneapolis, Minn.

SINCE the committee, appointed by the United States Public Health Service, on evaluation of serodiagnostic tests for syphilis in the United States, concluded its first report in 1935, this method, as first applied to spinal fluid, has been modified.[1] The technic, described here, renders the test for spinal fluid considerably more sensitive.

The unit of *unheated* spinal fluid, 0.2 c.c., is measured into a tube with a slightly smaller inside diameter as described for the serum test. (For spinal fluid the tube should preferably be 9 mm. by 75 mm., or with an inside diameter of about $\frac{6}{16}$ of an inch.) After the fluid has been placed in the tube, 0 1 c.c. of half saturated ammonium sulphate is added, and the rack is shaken for a few seconds. Then 0.1 c.c. of half saturated sodium chloride is added to each tube. Again the rack is shaken for a few seconds before the addition to each tube of 0.05 c.c. of antigen emulsion.[2, 3] The rack is then shaken for five minutes in the same manner as described for the serum test (at a rate of 275 oscillations per minute). The tubes are then centrifuged for fifteen minutes at a rate of 1,500 revolutions per minute. After centrifugation, 3.0 c.c. of 0.45 per cent sodium chloride are added to each tube, whereupon the tubes, one by one, are inverted 10 times without shaking the contents. Again the tubes are centrifuged, at a rate of 2,000 revolutions per minute, for three minutes. Then the fluid is decanted by completely inverting a handful of tubes, allowing the fluid to run vertically out of the tubes to the last drop, when the inverted tubes are lightly shaken once to allow complete drainage. To the sediment of each tube is then added 1.0 c.c. of 0.9 per cent saline. The individual tube is slowly inverted once or twice before the result is estimated.

A strongly positive reaction consists of large, irregular flocculate particles in a crystal-clear fluid. A weakly positive test shows smaller flocculate particles in a slightly hazy fluid. The negative reactions show a hazy fluid with unflocculated emulsion particles.

This procedure is in part based on the significance of the specific gravity of the mixture. The purpose of the ammonium sulphate is mainly the same as in the case of the serum test. The addition of half saturated sodium chloride, on the other hand, is primarily to increase the specific gravity. Both the shaking and the process of centrifugation are thereby rendered more

*From the Clinical Laboratories of the Minneapolis General Hospital.
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effective. During the first centrifugation (1,500 revolutions per minute for fifteen minutes), the emulsion particles are forced to the surface of the fluid due to the specific gravity involved. The antibody content is at the same time forced into unity with the emulsion. Addition of highly diluted sodium chloride (0.45 per cent) alters the specific gravity sufficiently for collecting the flocculate at the bottom of the tube during the last period of centrifugation. The "washing" of the emulsion or the flocculate by inverting the tube for a number of times before the last centrifugation, is necessary in order to allow the emulsion particles to separate in case the reaction is negative and flocculation has not taken place.

The use of a tube with a smaller inside diameter as recommended for the serum reaction, is necessary in order to prevent the flocculate from being washed away by decanting the fluid after the last centrifugation. The flocculate from spinal fluid appears to be somewhat more delicate than that from the serum reaction. (A tube 9 by 75 mm. is also satisfactory for the serum test.)

In the case of spinal fluid, the emulsion[2, 3] *must be prepared not more than one hour before use.*

By this method, 185 reactions have been compared with the Wassermann test as carried out in this laboratory. This flocculation method showed 59 positive reactions against 36 positive Wassermann tests on the same samples. Of the 59 positive cases by the flocculation method, 47 showed positive blood tests, and 8 patients with negative blood tests had a definite syphilitic history. Two patients with some symptoms of neurosyphilis, remain, at this time, unverified by clinicians.

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A SIMPLE AND INEXPENSIVE DEVICE FOR FILLING CULTURE TUBES AND BOTTLES*

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THE dispensing of definite quantities of culture media and of water for dilution purposes into tubes and bottles is a time-consuming process. Numerous devices to facilitate the work have been suggested. For some years in our laboratories, overflow pipettes of glass, made in pairs and so arranged that one is filling while the other is emptying, have been used in dispensing 9 and 99 c.c. of water used for dilution purposes. Prickett† has described a somewhat similar device which, since it is made of metal, is preferable to glass, and which has the advantage of being easily adjustable so as to deliver different volumes.

During the past three years, a set of very simple devices has been used in our laboratories for the same purpose. The device has established itself with the entire staff, proof of its value.

During recent years, heavy glassware has replaced much of the chemical glassware formerly used, especially for the storage of media and as a substitute for the Petri dish. The particular type of container employed is either a 6-ounce or a 12-ounce prescription bottle with threaded neck, known as the Illini-Oval made by the Owens-Illinois Glass Company. This bottle has one flat side, the other being slightly crowned. The area of the 6-ounce bottle is approximately that of the usual Petri dish. Screw caps of aluminum are used for closing the bottles. The liners of the caps are of pulp with an oil paper cover. In ordinary laboratory work, the liners are removed from the caps to avoid trouble with the liners sticking to the tops of the bottles to which they are tightly drawn when the bottles are cooled after sterilization. If lined caps are to be used, they should not be screwed tightly previous to sterilization. The unlined caps supply a sufficiently tight closure to decrease evaporation to such an extent that material can be stored for weeks with so little loss in volume as to be of no significance and with almost complete prevention of contamination on storage. Culture media and water are dispensed into these bottles by means of a V-shaped funnel of sheet metal, preferably of Monel metal, or of some resistant alloy. Each such funnel is provided with two partitions, thus making three compartments, each of which is provided with a cylindrical exit tube. The spacing of the tubes is such that when three bottles are grasped with the hand so as to hold them against each other, the openings of the necks will be spaced the same as the tubes, thus making the task of placing the funnel in position no more difficult than is the case with a single tubed funnel.

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†Am. J. Public Health 25: 618, 1935.

The liquid is filled into the bottles through the multiple funnel by a multiple dipper illustrated in Fig. 1. The individual dippers are so spaced on the carrying arm that each dipper will empty into a compartment of the funnel. The individual dippers are made to deliver the desired volume when they are completely filled. But one funnel is needed for any one type of container. Dippers of varying capacity adapted to the funnel spacing are needed. In our laboratories, dippers of 15 c.c. capacity are used for filling nutrient agar into the

Fig. 1.

6-ounce bottles, which are to be used as a substitute for Petri dishes, and dippers of 49 and 99 c.c. capacity for measuring water for dilution purposes. A smaller funnel and accompanying dipper are used for placing 9 c.c. of water into ordinary culture tubes, again for dilution purposes.

The scheme is not desirable for placing culture media into tubes, due to the soiling of the inner wall of the tube near its top, thus causing the cotton to adhere to the glass.

The 12-ounce bottles are used for the growing of mass cultures of bacteria for the preparation of antigens to be employed in the diagnosis of Bang's disease in cattle, and for the storage of media, for which purpose they can be filled three-fourths full without trouble when sterilized in the autoclave.

The substitution of a bottle costing from one-sixth to one-tenth as much as a Petri dish and for expensive chemical glassware has helped our laboratories to maintain volume of work in spite of a decreased operating budget.

The glass withstands repeated heatings in the autoclave without breaking. Approximately fifteen hundred of such bottles have been autoclaved twice per week for eight months with negligible breakage. In many cases, the bottle, as a substitute for the Petri dish, has marked advantages, especially in the case of cultures to be incubated for a prolonged period of time. With the unlined caps, there is sufficient ventilation and yet evaporation is so diminished that cultures can be kept for weeks, and the contamination, so certain to result with Petri dishes on prolonged incubation, is almost absent.

EXAMINATION OF MOUSE OVARIES IN THE ASCHHEIM-ZONDEK TEST FOLLOWED BY CASTRATION FOR THE QUANTITATIVE TESTING OF ESTROGENIC SUBSTANCES*

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MANY laboratory workers can make use of a simple procedure which in one operation allows the diagnosis of the Aschheim-Zondek test and at the same time enables one to castrate the animals in preparation for use as testing animals for estrogenic substances.

After the routine Aschheim-Zondek test injections, the mice are anesthetized singly with ether. The mouse is placed on its abdomen and a dorsal incision is made through the skin. The incision extends about three-fourths of an inch running along the lumbar part of the spinal column. The skin is retracted and each ovary is easily located by making a nick in the lumbodorsal fascia lateral to the spinal column and by cutting a small opening in the lumbar muscles. This discloses the kidney. The ovary is found contiguous to the kidney at its inferior pole, imbedded in folds of fat. The fatty fold is drawn through the opening in the muscle and the ovary is clamped, ligatured, and excised. A thorough examination of the salpingian fat is made for the possibility of finding any accessory ovarian tissue. The exposed structures are then replaced and flaps of muscle are brought together, no stitches being necessary. Then the other ovary is similarly removed from the other side of the animal. Before the incision is closed the ovaries are placed between two glass slides and examined under low power. The skin is closed with three or four interrupted sutures of black silk,

*From the Departments of Medicine and Clinical Pathology of the French Hospital.
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making the bilateral oophorectomy complete. A trained operator can perform the operation in approximately eight minutes and even though sterile conditions are not maintained, the mortality is negligible.

With this technic, not only can the Aschheim-Zondek test be performed as accurately as by any other method, but theret is no need to kill the mice when they can be so easily castrated with little extra effort. After castration the mice are allowed to convalesce and the sutures are removed on the fifth or sixth day with or without ether anesthesia. When the animals will have completely recovered from the surgical procedure and will have become mature, they may be used in the testing of estrogenic substances and in quantitative estrin determinations.

SUMMARY

A simple method of examining immature mouse ovaries for results of the Aschheim-Zondek test with subsequent surgical removal of the ovaries in one operation has been described. This single procedure produces castrates useful in estrogenic determinations and eliminates two operations and two separate sets of animals. The technic is simple, time-saving, and economical, in view of the large number of mice needed for quantitative estrin determinations.

COMPLETE POSTMORTEM EXAMINATIONS THROUGH SURGICAL WOUNDS*

S. H. Polayes, Ph.B., M.D., Brooklyn, N. Y.

MOST pathologists at some time have been confronted with the task of removing viscera per rectum when permission for a postmortem examination is granted with the proviso that no visible skin incision be made. Frequently advantage may be taken of the presence of operative wounds through which all the viscera can be obtained for examination, and permission for such an examination can often be secured without any difficulty. When the wound is in the chest or abdomen the task is quite a simple one. This is not common knowledge among clinicians who, if properly informed, would make more frequent attempts to secure permission for a wound inspection when they fail to get consent for an examination through the usual anterior skin incision. If the wound happens to be in a more remote location in the body, then certainly little, if any, effort is made to secure permission for a postmortem wound inspection. The attention of the physician should be called to the fact that it is possible to perform a postmortem examination through a surgical wound in the head or neck. I wish to describe such a procedure lately employed in the case of an adult male, on whom a mastoid operation and jugular bulb ligation had been performed and for which permission for a postmortem wound inspection and examination of viscera was granted with the provision that no chest or abdominal skin

*From the Departments of Pathology, Cumberland Hospital and Jewish Hospital of Brooklyn.

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incisions be made. A complete postmortem examination was performed in which not only were the thoracic and abdominal organs resected but all the pelvic structures as well, including the prostate. By moderate stretching of the margins of the wound (jugular sinus and mastoid incisions) until the opening admitted the hand, sufficient space was made for any desirable manipulation of the neck organs. A "laryngectomy" was performed, giving free access to the sternoclavicular joints which were then severed and the thorax easily entered. Complete evisceration of the thoracic organs was found to be a relatively simple task. The diaphragm was then incised on each side and the intestines delivered through the wound. The remaining abdominal viscera, with the exception of the liver, were readily removed in a similar way. The liver had to be divided into three parts to enable its complete removal. The organ was so divided as to permit one portion to remain attached to stomach, mesentery, and pancreas. The pelvic structures were removed with a little more difficulty, but nevertheless completely and intact. The entire prostate, bladder, and rectum were freed and removed en masse. With a little more effort the testes, were it absolutely necessary, could have been removed also.

From the cephalic end, almost as complete an examination was performed through the same wound. By reflecting as much of the incised scalp as possible without additional incision, and by sawing off a sufficient amount of bone to admit four fingers, the tentoria cerebri et cerebelli were resected from their attachment to the skull and the cranial nerves severed. Then by careful manipulation of the hemisphere the entire cerebrum was shelled out, only slightly disfigured. Difficulty was encountered in removing the brain in toto, so that the pons and cerebellum had to be severed from the cerebrum in order to avoid maceration of the former. On removal, however, these structures were found to be sufficiently well preserved to permit of detailed examination. With the brain removed there was enough space left to make it possible to resect the pituitary and also to make any other necessary observations of the cranial vault, such as examination of the opposite middle ear and accessory nasal sinuses.

I was rewarded for my efforts in finding the following: thromboulcerative endocarditis with septic infarction of the lung, spleen and kidneys; purulent pleuritis; duodenal ulcer (unsuspected); and purulent otitis media.

The important findings in this case illustrate the value of the examination and justify the plea which I wish to make: not to despair of securing a postmortem examination in any postoperative case in which permission for the usual chest and abdominal skin incision for a complete autopsy is not granted. A request for a wound inspection should always be made by the attending physician and with a little skill the pathologist may make a satisfactory examination. Needless to state, such an examination should not be attempted without the knowledge and consent of the individual who is legally authorized to grant the permission. Such permission can be obtained in a large number of cases offering problems in diagnosis which only a postmortem examination can solve, but which have followed the body to the grave as unsolved problems because efforts have not been made to secure permission for a modified postmortem examination.

THE QUANTITATIVE ESTIMATION OF PROTEIN BY THE RAPID METHOD OF KERRIDGE*

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THE accuracy of the gravimetric and Kjeldahl methods for determining the quantity of protein in biologic fluids is well recognized, but their clinical usefulness is considerably diminished by technical requirements. The demand for simpler methods has called forth a variety of procedures, all of which may sacrifice a certain degree of accuracy in the interest of easy performance. Most clinical requirements can be satisfactorily met by determinations that fall within 10 per cent of the true value, but it is doubtful if any of the proposed substitutes which have any claim for simplicity consistently give figures as close as this.

For the rapid determination of protein in urine, there are available several well-known and rather simple methods. One is the refinement of Tsuchiya's sedimentation method introduced by Shevky and Stafford,[1] wherein the volume of protein precipitated by an alcoholic solution of phosphotungstic and hydrochloric acids is read directly after centrifugation in a specially calibrated centrifuge tube. The authors report that 30 comparisons with Kjeldahl analyses gave an average error of 8.4 per cent and a standard deviation of about 10 per cent. In our experience the error was usually somewhat greater than this, and we have found the method subject to very wide deviations when the temperature fluctuates widely. In our series of 8 duplicate determinations, 4 showed positive errors of from 15 to 25 per cent.

There are also several modifications of the method of Folin and Denis[2] which compare the turbidity produced by adding sulphosalicylic acid to the unknown with that similarity developed in known concentrations of sheep serum. To obviate the necessity of renewing the standard frequently, Kingsbury[3] proposed the use of permanent formazin-gelatin standards. The standards seem difficult to make and the method has not been widely used. Subsequently Lashmet and Newburgh[4] suggested the use of an alkaline solution of cupric sulphate for the same purpose, and Gibbons[5] has affirmed the value of their procedure, but neither author presented data concerning its accuracy. We have been quite unable to achieve even moderately satisfactory results with it. It is our feeling that the method of Shevky and Stafford is the more reliable of the two.

For the rapid determination of plasma proteins, we are aware of only one method that has given consistent results. Moore and Van Slyke[6] have studied the correlation existing between the protein content and the specific gravity

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of plasma and have described a technic for measuring the latter which they say gives a maximum error of 0.6 gm. of protein per 100 c.c. of plasma. In the edema zone of plasma proteins this would entail a possible error of more than 10 per cent, but the method is undoubtedly useful if care is taken to make the proper temperature corrections.

In 1931 Kerridge[7] described an exceedingly simple method for determining the protein content of urine and spinal fluid which appeared to be satisfactory. Apparently it has attracted little attention in the American literature, and we have thought it worth while to report that we have been able not only to confirm her experience but to extend the technic to such material as plasma and transudates with results that closely approximate those given by the micro-Kjeldahl procedure.

METHOD

A suspension of India ink is added to a suitable quantity of the material to be analyzed, the protein in it is precipitated with trichloracetic acid, and the grayness of the resulting mixture matched against a series of standards previously prepared in exactly the same manner. Since the quantity of carbon is constant, the shade of the mixture will depend directly upon the amount of protein present.

Standards.—We have preferred to use an initial volume of 5 c.c. rather than the 1 c.c. which Kerridge proposed and to arrange the standards somewhat differently, but this is purely an individual matter. Our standards were prepared from fresh ox plasma, the protein content of which was determined by the usual macro-Kjeldahl technic. Into each of 14 small uniform test tubes was placed an amount of the plasma which, when diluted to 5 c.c., made a solution of the desired concentration. For clinical purposes we found the following arrangement satisfactory: blank, 0.025, 0.05, 0.075, 0.25, 0.5, 0.75, 1.0, 1.25, 1.5, 1.75, 2.0, 2.5, and 5.0 gm. protein per cent. The volume in each tube was brought up to 5 c.c. with distilled water; control tubes showed that nothing is gained by using 0.9 per cent saline as a diluent. Then to each tube was added 0.5 c.c. of a 1:25 dilution of Higgin's eternal ink and, after mixing, 0.5 c.c. of 100 per cent trichloracetic acid. If the contents are then thoroughly mixed by vigorous shaking, the various shades of grayness can be easily distinguished, and between the fifth and the ninth tubes there is no difficulty in interpolating a reading to 0.13 gm. per cent. Such standards have kept for more than five months without deterioration.

Urine.—All samples should be filtered unless perfectly clear. It is usually unnecessary to make a preliminary dilution but differences in shade are distinguished with minimum error in the midportion of the standard scale, so that occasionally it may be necessary to make an appropriate dilution after a preliminary reading has given an approximate estimate. In any event 5 c.c. of the unknown are mixed with 0.5 c.c. of the ink suspension and treated with 0.5 c.c. of the precipitant exactly as in the case of the standards. A reading can thus be obtained in less than five minutes, and independent observers usually check within 0.1 gm. per cent. Unless a dilution has been made, no calculations are involved.

Serum.—Plasma or serum is best read at a 1:10 dilution. Accordingly, 0.5 c.c. is brought up to 5 c.c. with water, the ink and acid added as described above and the reading multiplied by the dilution factor.

Spinal Fluid.—Because large amounts are not often available, we have adopted Kerridge's original specifications which call for 1 c.c. of material. Test tubes measuring 175 by 10 mm. were used and the protein concentrations of the nine chosen standards were as follows: 0, 25, 50, 75, 100, 150, 200, 250, and 300 mg. per cent. Ink and acid were added from 0.1 c.c. blood sugar pipettes, the total volume in each tube being, therefore, 1.2 c.c. Should a specimen unexpectedly contain more than 0.3 per cent protein and no more be available for preliminary dilution, a reading may be made by adding 1.1 c.c. of water and 0.1 c.c. of ink (or the required multiple thereof) to the original mixture.

Transudates and Exudates.—Here the method meets its most serious limitation. It is notoriously difficult to clarify chylous effusions and unless the fluid is reasonably clear, results will be high. Filtration through porcelain will frequently remove the finely emulsified fat, but this is so laborious that other methods are preferable if the fluid is typically milky and cannot be cleared by passage through filter paper. Either the small or the large standards may be used, depending upon the amount of available lymph.

RESULTS

The values for serum proteins* upon which our conclusions are based were obtained by the usual micro-Kjeldahl and nesslerization procedure. Several simultaneous checks by the macro-Kjeldahl method showed agreement to within 3 per cent. The proteins in urine were precipitated with tungstic acid and the nitrogen content of the purified redissolved precipitate determined colorimetrically by micro-Kjeldahl analysis.[8] Repeated checks by the gravimetric method showed an average deviation of about 2 per cent.

Urine.—Thirty-four consecutive samples have been independently analyzed by the two methods indicated (Fig. 1). Of these, 20 showed agreement to 5 per cent, and in only 8 was the error greater than 10 per cent. The average error for the series was + 2.5 per cent, and the mean deviation from this average error, the sign being taken into account, was ± 6.5 per cent. The protein content ranged from 0.92 to 14.2 gm. per liter.

Serum.—It is evident that any method which determines only the total proteins of serum or plasma is of limited usefulness, and we do not wish to overemphasize the applicability of the Kerridge method to blood. Its relative accuracy, however, was tested on 17 samples of human serum whose protein content ranged from 2.1 to 8.1 gm. per cent. In only two instances was the deviation from the micro-Kjeldahl analysis as great as 11 per cent, and in 9 of the remaining 15 the error was 5 per cent or less. For the series the average was + 3.0 per cent, and the mean deviation from this average error ± 4.4 per cent.

*We are indebted to the Department of Pediatrics for some of the Kjeldahl analyses of serum and urine upon which these results are based.

The reddish tinge produced by excessive hemolysis may be largely eliminated by increasing the initial dilution to 1:50. A moderate degree of lipemia introduces no significant positive error.

Spinal Fluid.—The method is less exact when applied to such quantities of protein as are contained in normal spinal fluid, but this objection holds also for any method. Because of the relative inaccuracy of methods employing the Kjeldahl procedure at these low protein concentrations, we have preferred to work with known protein solutions rather than to compare simultaneous analyses of spinal fluid by the two methods employed above. To this end, 1 c.c. portions of 12 different dilutions of horse serum whose protein content

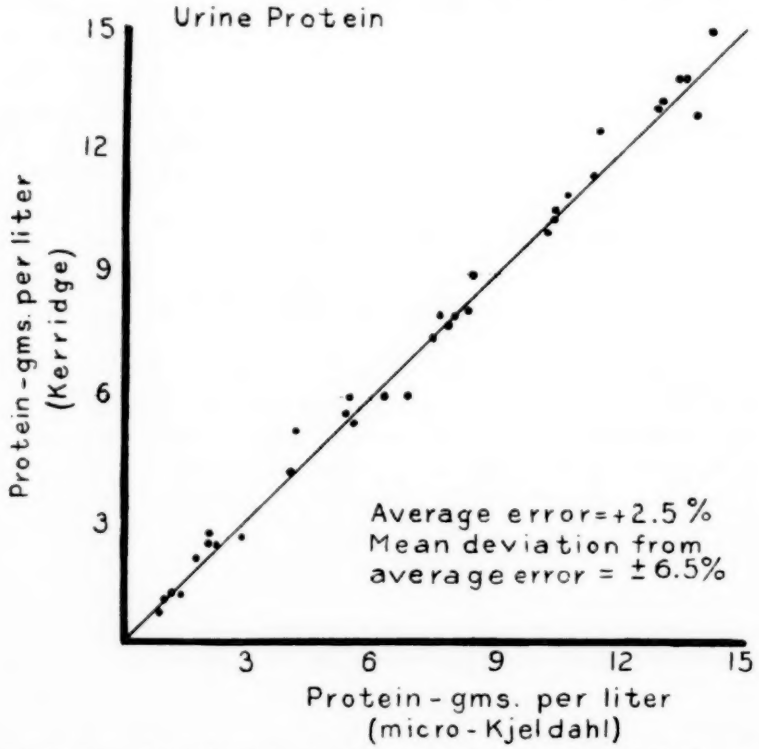

Fig. 1.—Simultaneous determinations of urine protein by the micro-Kjeldahl and Kerridge methods.

was known from macro-Kjeldahl analysis were treated in the manner indicated and read against the smaller standard tubes. The results appear to indicate that the method is sufficiently accurate for clinical purposes:

PROTEIN, MG. PER CENT		PROTEIN, MG. PER CENT	
KNOWN	FOUND	KNOWN	FOUND
47	56	40	38
61	69	31	25
40	38	36	31
54	62	58	56
34	25	63	69
47	46	45	38

Marked xanthochromia does not interfere with the Kerridge determinations.

Exudates and Transudates.—We have not analyzed a large enough number to warrant a detailed report but have obtained entirely similar results on several samples of each. The difficulty with chylous effusions has been mentioned.

SUMMARY

Kerridge's method for the rapid quantitative estimation of protein has been applied to urine, plasma, spinal fluid and nonchylous effusion fluid with results that seem superior to those obtained by any of the simple methods in common use. The error, as judged by the micro-Kjeldahl method, is less than 10 per cent.

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A NEW INSTRUMENT FOR DETERMINATION OF VENOUS PRESSURE BY DIRECT METHOD*

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THE direct method of venous pressure determination is not a new procedure. It was done as early as 1910 by Moritz and v. Tabora,[1] who were followed by a number of other workers, Fuchs,[4] Schott,[3] Bedford and Wright,[5] and others.

The reader is referred to Eyster[2] *The Clinical Aspects of Venous Pressure* and other excellent sources for a consideration of the value and indications for the use of venous pressure determination. The prime objection to this procedure has been the danger and discomfort of venipuncture. However, intravenous manipulation as practiced today in hospital and office routine has almost eradicated this objection.

The instrument consists of an 18 or a 21 gauge short bevel needle to which is fitted a three-way valve system, and a receptacle for a glass manometer. The

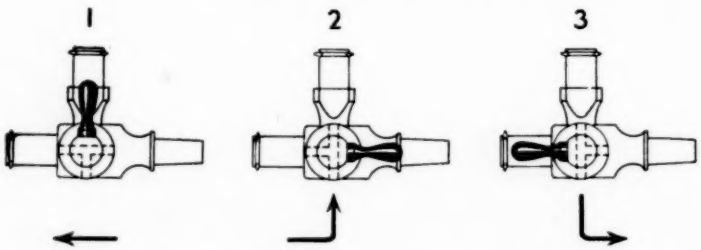

Fig. 1.—*1*, Direction of flow from vein to syringe. *2*, Direction of flow from syringe to manometer. *3*, Direction of flow from manometer to vein.

glass manometer is calibrated to a total of 32 cm. (with an extension to a total of 48 cm.) and is attached to the adaptor in the upright position by means of a Luer lock system. A 10 c.c. syringe completes the equipment. When the manometer is affixed to the adaptor in its receptacle and the syringe is attached to the adaptor by means of the three-way fitting of the valve, blood can be withdrawn from the vein into the syringe, containing either sterile saline or citrate solution, then the manometer is filled with this mixture, and by the third adjustment of the valve, the direction of the flow is changed from the manometer to the vein.

The procedure adopted is as follows: the patient is kept at rest for a period of fifteen minutes before the test. The right forearm is supported at the level of the right auricle and the antecubital fossa is prepared in the usual manner. A sterile 10 c.c. syringe containing 5 c.c. of sterile 3 per cent sodium citrate solution is attached to the needle which is introduced into any suitable vein in the area, and a few cubic centimeters of blood are drawn into the syringe. For

*From the Coney Island Hospital and the Jewish Hospital.
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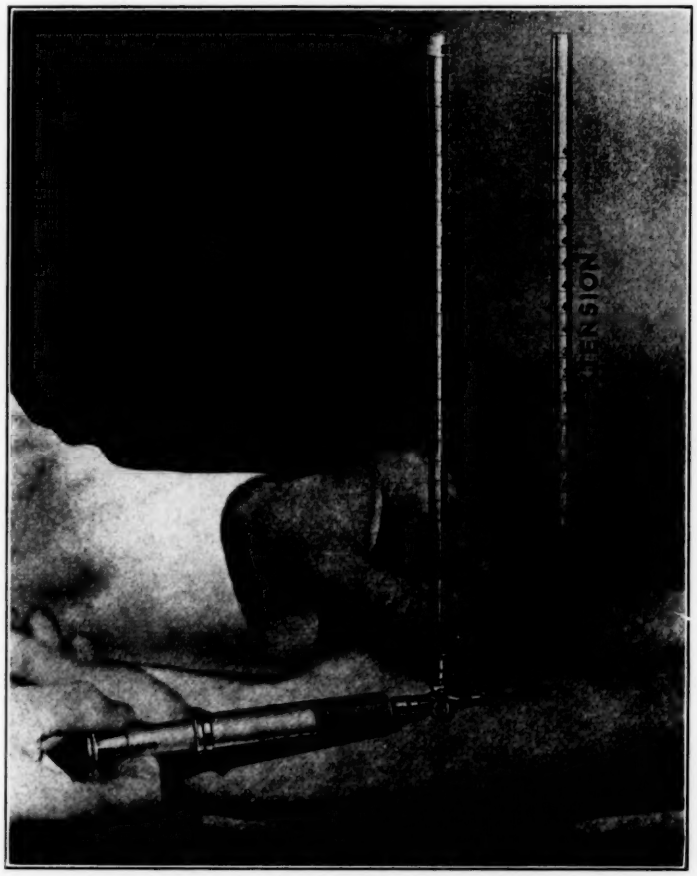

Fig. 2.—Instrument with needle in vein.

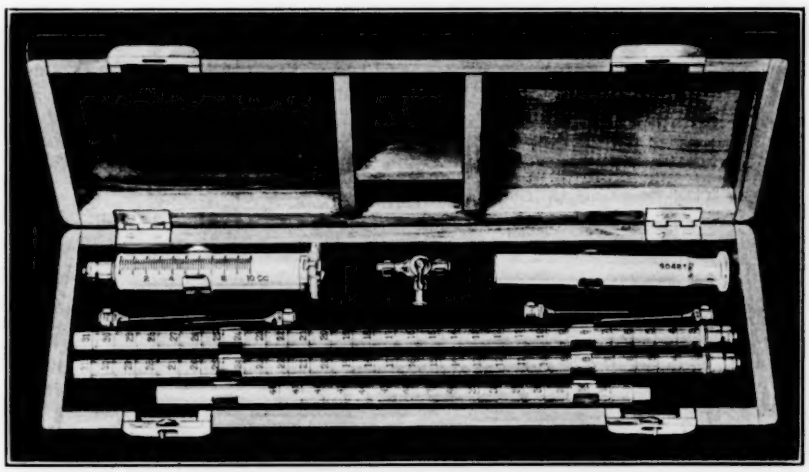

Fig. 3.—Instrument in compact carrying case.

this stage the valve must be kept in Position 1 (see diagram). The manometer is then affixed to its receptacle, the valve is put in Position 2 and is filled by injecting the contents of blood and citrate already present in the syringe. The valve is then set in Position 3 and the aforementioned mixture is allowed to run into the vein. The level at which the fluid rests is read directly on the manometer tube as the venous pressure. The Valsalva phenomenon, expiratory effort with the chest held rigid in inspiration, is now applied to determine the continuity of the manometer with the venous stream. This will cause the venous pressure to rise markedly.

The entire procedure can be performed in five minutes, and requires no assistance. The advantages are the ease with which the readings can be determined, the firm attachment of manometer to adaptor without danger of breakage when glass is directly fitted to metal, the ease with which this instrument can be cleaned, and finally by means of the valve system, drugs may be introduced into the circulation for study of the effects without interrupting the manometer system. It is in this latter feature that this instrument differs from other instruments now being used.

Results obtained with the use of this instrument readily agree with the figures quoted by other workers. Normal variations of venous pressure have fallen in range between 60 and 120 mm. In cases of heart failure the figures have ranged as high as 400 mm. in my experience. Repeated determinations have been done at short intervals without any ill effects.

SUMMARY

1. A new instrument is described for direct venous pressure determination.

2. Its advantages are simplicity of procedure, firm attachment of manometer system, and the ease with which the instrument can be kept clean.

3. The instrument allows the introduction of venous medication without being detached, so that the effects of drugs on venous pressure may be studied.

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1299 Ocean Avenue

THE HINTON TEST FOR SYPHILIS*

The Second Study of Its Clinical Value in 3,000 Patients

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Charles L. Schmitt, M.D., Pittsburgh, Pa.

LAST year[1] we reported our findings on the comparative value of four laboratory procedures, the Wassermann (lipoid antigen), the Wassermann (cholesterinized antigen), the Kahn, and the Hinton in a study of 3,000 consecutive patients. We arrived at the following conclusions:

1. That the sensitivity of the Hinton test in the serologic investigation for syphilis was very much greater than any of the others.

2. That each of the four procedures brought to light cases which otherwise would have remained unrecognized.

3. That in a thorough survey for syphilis all of the four laboratory tests should be performed.

We have again completed a comparative study along the same lines in a new group of 3,000 consecutive patients and wish to present our findings in comparison with our previous report. To all intents and purposes our conclusions remain practically the same.

In this report the tables designated with Roman numerals refer to our previous, our first report; the tables designated with Roman numerals and the letter A refer to our later findings.

Table I

General Summary

	I	I A
Total number of individuals tested	3,000	3,000
Number of positives to one or more tests	655	622
Number of doubtful to one or more tests	16	11
Number of negatives to all tests	2,329	2,367

Table II

Comparison of the Methods Used

	II		II A	
	POSITIVE	ANTICOMP.	POSITIVE	ANTICOMP.
Wassermann lipoid	317	6	322	1
Wassermann cholesterol	362	6	378	1
Kahn	400	0	505	0
Hinton	643	0	582	0

*From the Pittsburgh Skin and Cancer Foundation.
Received for publication, January 18, 1936.

TABLE III

ANALYSIS OF THE POSITIVE REACTIONS

WASSERMANN LIPOID	WASSERMANN CHOLESTEROL	KAHN	HINTON	III	III A
+	+	+	+	297	316
+	+	−	+	15	0
+	+	+	−	1	0
+	+	−	−	1	3
+	−	−	−	1	1
+	−	+	+	1	5
−	+	+	+	33	48
−	+	+	−	1	0
−	+	−	+	6	3
−	+	−	−	5	4
−	−	+	+	61	126
Anticomp.	Anticomp.	+	+	3	0
−	−	+	−	3	7
−	−	−	+	227	109

TABLE IV

ANALYSIS OF THE HINTON ONLY POSITIVE PATIENTS

HISTORY	PHYSICAL FINDINGS	PREVIOUS ANTISYPHILITIC TREATMENT	IV	IV A
+	+	+	137	86
+	+	−	16	5
+	−	−	12	2
−	+	+	2	2
−	+	−	7	2
−	−	+	11	1
−	−	−	42	11
		Total	227	109

TABLE V

ANALYSIS OF THE UNCONFIRMED HINTONS

	V	V A
Number	42	11
Spinal fluid Wassermann positive	23	1
Remaining unconfirmed	19	10

TABLE VI

ANALYSIS OF NEGATIVE HINTONS—POSITIVE TO OTHER TESTS

WASS. LIP.	WASS. CHOL.	KAHN	HISTORY	PHYSICAL	PREVIOUS TREATMENT	VI	VI A
+	+	+	+	−	+	1	0
+	+	−	+	−	+	0	1
+	+	−	−	−	−	1	2
+	−	−	−	+	−	1	0
+	−	−	−	−	−	0	1
−	+	+	+	−	+	1	0
−	+	−	+	−	+	3	2
−	+	+	−	−	+	1	0
−	+	−	−	−	−	2	2
−	−	+	+	−	+	0	3
−	−	+	−	+	−	0	2
−	−	+	−	−	−	2	2
					Total	12	15
					Considered unconfirmed	4	5
					Hinton failed in	8	10

THE COMPARATIVE VALUE OF THE HINTON TEST

In the second group of 3,000 patients we found 622 serologically positive individuals. Of these, 582 gave a positive Hinton reaction. The test giving the closest number of positives was the Kahn with 505.

Of the 109 patients who were negative to other serologic tests but positive to the Hinton test 99 were proved to be syphilitic. Ten cases remained unconfirmed and are classified as false positives. All of the other tests combined produced 5 unconfirmed cases.

The Hinton test failed in 10 cases which were positive in one or more of the other tests. The 3 other tests combined failed in 99 cases.

Comparing the results of our first and last study two outstanding differences were obtained:

1. A large increase in the Kahn positive patients from 400 to 505.
2. A large reduction of the Hinton alone positive patients from 227 to 109.

SUMMARY OF THE TWO STUDIES

In 6,000 patients 1,277 individuals gave a positive reaction to one or more of the four laboratory procedures used; 27 gave a doubtful result and 4,696 were entirely negative.

Of the 1,277 positive cases the Wassermann lipoid was positive in 639, the Wassermann cholesterol in 740, the Kahn in 905, and the Hinton in 1,225.

Of the 1,277 serologically positive cases 38 remained unconfirmed (being positive to one type of serological test only); 1,239 or 20.6 per cent of the 6,000 consecutive patients examined gave positive evidences of having demonstrable syphilis.

This result was obtained by performing multiple serologic examinations (at least four tests) on each individual examined. Each test directed us to the finding of cases which otherwise would have been missed.

CONCLUSION

Further studies substantiate the premise that all available tests should be utilized in the establishment of the diagnosis of syphilis in order to give the best possible service in syphilis.

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1. Hollander, L., Schlesinger, C. R., and Schmitt, C. L.: The Hinton Test for Syphilis, Urol. & Cutan. Rev. 39: 617, 1935.

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DEPARTMENT OF REVIEWS AND ABSTRACTS

ROBERT A. KILDUFFE, M.D., ABSTRACT EDITOR

CANCER: The Value of the Macronucleolus in the Cancer Problem, Mac Carty, W. C. Am. J. Cancer **26**: 529, 1936.

Mac Carty strongly advocates the examination of fresh tissues and describes the Macronucleolus as follows:

The nucleolus is much larger in proportion to size of the nucleus in all malignant cells, regardless of the type or origin of the neoplasm, this difference being great enough to permit easy differentiation from all other cells in the hands of one experienced with fresh tissues.

The enlargement can be seen clearly only in fresh tissues which have not been embedded by present-day histologic methods.

The macronucleolus is unquestionably diagnostic for malignancy, the only exception being neurocytes and ova, which are the only normal human cells containing large nucleoli. Such cells rarely if ever occur as the main constituents of malignant neoplasms.

By accurate measurements of resected malignant neoplasms it has been seen that the medical profession has made little progress in the early recognition of cancer. Therefore the profession should welcome this new means of making early diagnoses.

Cancer is being recognized only in its late stages just as tuberculosis was formerly recognized only in its late stages, clinically known as consumption, scrofula and phthisis.

The presence of malignant cells can now be recognized in chronic inflammatory conditions which are the sites of origin of all of the earliest cancers thus far recognized.

Members of the medical profession, especially pathologists, must begin to look for the macronucleolus, which is easily found in fresh tissues, if the diagnosis is to be made early, just as they look for tubercle bacilli in all chronic inflammatory conditions when hoping to recognize tuberculosis in its earliest and curable stage. Until pathologists learn to study fresh tissue there will be no such thing as recognizing cancer in its early stages.

LUNGS: A Study of 57 Cases of Bronchogenic Carcinoma, Rosedale, R. S., and McKay, D. R. Am. J. Cancer **28**: 493, 1936.

In the past ten years 466 cases of malignant disease were autopsied at the Buffalo City Hospital. Bronchogenic carcinoma constituted 7.5 per cent of these.

In this district this tumor appears to predominate in people employed in irritating atmospheric conditions.

Bronchogenic carcinomas are situated most frequently at or near the lung hilus, commonly taking origin in a first order bronchus. They occur usually as a single massive lesion at one hilus in contrast to the multiple bilateral peripheral nodules of metastatic tumors.

Histologically the tumors in this series consisted of various predominant cell types. Round or spindle cells were found in all cases.

Bronchogenic carcinoma may metastasize widely. The regional lymph nodes were involved in all our cases.

Clinically the symptoms produced by these tumors closely simulate other diseases of the lungs, such as tuberculosis, pneumonoconiosis, and bronchiectasis.

Roentgenographic study may be of aid in differentiating between the several diseases simulating tumor; but in the presence of secondary pulmonary or pleural pathology the diagnosis may not be suspected.

Because of this and other reasons bronchoscopy with removal of tissue for microscopic examination is a most valuable procedure.

The authors feel, from the study of their material, that bronchogenic carcinoma occurs frequently enough for it to enter the differential diagnosis of all obscure chest diseases in individuals over thirty years of age.

PHOTOGRAPHY: A Universal Developer, Schneckenberger, M. G. J. Biol. Photo. Assn. **4:** 170, 1936.

1. Mix exactly as follows:

Boiling water	about 12 oz.
Hydroquinone	1 oz.
Metol	1 oz.
Pyro	1 oz.

Add one at a time in the order given to the boiling water and continue to boil at least one minute.

2.

Cold or cool water	about 15 oz.
Sodium bisulphite	1 oz.
Potassium bromide	¼ oz.

For a stock solution add No. 1 to No. 2 and enough water to make 1 quart.

For use:

Water	1 quart
Carbonate of soda	2 oz.
Sulphite of soda	1½ oz.
Stock solution No. 779	1 oz.

PNEUMONIA, Lung Puncture in Lobar, Sappington, S. W., and Favorite, G. O. Am. J. M. Sc. **191:** 225, 1936.

With a simple and apparently safe technic, 60 cases of lobar pneumonia (57 pneumococcic and 3 streptococcic), were subjected to diagnostic lung puncture. Positive cultures, suitable for typing, were obtained in 90 per cent, half of these within six hours. Lung puncture cultures made three and twenty-four hours after the administration of antipneumococcus serum were positive. In 25 cases in which both the lung and sputum pneumococcus were typed, there was 100 per cent agreement. Where sputum is at once available, therefore, lung puncture is unnecessary. In 22 of the cases, however, the sputum was either absent or unobtainable at the time the lung puncture was made. The method is, therefore, recommended for early diagnosis and typing when sputum is not as quickly available.

The method used follows:

In general, after preliminary cleansing of the skin and anesthetization of the underlying tissues with 0.5 per cent procaine solution the consolidated lung is punctured with a long needle attached to a syringe which may or may not contain broth or saline. Strong suction is made, and the resulting withdrawn material distributed to culture media. The skin is usually cleansed with iodin and alcohol. In most cases local anesthesia is recommended but the authors did not find it necessary.

The location of the consolidated area was carefully determined by physical signs and roentgen ray. Puncture was not done unless there was definite evidence of pneumonia. Over this area of maximum signs and shadow, the puncture was made. This usually was over the posterior inferior aspect of the chest, but the lung was frequently entered without damage through the upper chest posteriorly or anteriorly (infraclavicular region) or in the axilla. The skin over the prospective site was thoroughly swabbed with alcohol only. No anesthetic was used and patients made little or no complaint. A dry 5 c.c. glass syringe with a 6 cm. No. 20 needle was employed. The needle was entered 5 or 6 cm. and strong suction made on withdrawal. The needle, after introduction, was not moved about or changed from its primary position in the lung except to withdraw it. If negative pressure was encountered on suction the results were usually good; if positive pressure was found and the piston of the syringe

slipped back easily, the results were usually disappointing. Commonly a little bloody matter was obtained. This might be only a drop or two or as much as 1 c.c. Not infrequently nothing grossly visible was removed or a mere serous moisture. Occasionally just before complete withdrawal a little clear fluid entered the syringe, evidently a thin pleural exudate, In this instance, positive cultures were not always obtained. After the needle was removed from the lung, the contents of the syringe were at once washed into a single tube of slant agar at the bottom of which were 1.5 c.c. of plain broth pH 7. This was done by entering the small 5 c.c. syringe and needle into the agar tube so that the needle reached to the bottom of the tube. The broth was then sucked up into the syringe and expelled, and this was repeated 4 or 5 times. Even when there was no visible withdrawn matter the procedure was followed and positive cultures were not infrequently obtained. Especially was this prospect good if a few fibrin flakes were seen. The tube was at once incubated and examined at short intervals later, say two, four, six and twelve hours, by making spreads of the broth at the bottom of the slant and the agar surface just above it.

The first evidence of growth, if the examination of the broth was made only a few hours after the puncture, was at times only a few pneumococci. At other times, the first examination showed numerous organisms. After their first appearance, even in very small numbers, the pneumococci increased very rapidly. As soon as they were in sufficient numbers for typing, this was done by the Neufeld method, using a small drop of broth against one or two of serum. A culture was considered ripe for typing when there were at least 10 bacteria per oil immersion field. Fewer bacteria, when diluted with typing serum and methylene blue, required too tedious a search to find the organisms. Pneumococci cultured this way showed beautiful capsulation under the action of the serum in primary cultures as young as two hours or as old as thirty-six hours. The secondary growths did not show it. When the primary growth was injected into a mouse, the peritoneal wash also showed excellent capsulation with serum.

BLASTOMYCETES, Detection of, Nomland, R. Arch. Dermat. & Syph. 32: 924, 1936.

Nomland uses the method following:

A micro-abscess in the sloping border of the skin is pierced, and the pus is picked up on the point of a sharp knife. It is then transferred to a slide and mixed with a small amount of tap water; a cover glass is pressed on, and the material is examined with the iris diaphragm on the Abbe condenser almost closed. Water is superior to solutions of sodium hydroxide because water does not form artefacts such as are made by the interaction of sodium hydroxide and fats in the specimen.

GLOMERULAR EFFICIENCY, Sodium Ferrocyanide as a Clinical Test of, Stieglitz, E. J., and Knight, A. A. J. A. M. A. 103: 1760, 1934.

The Titration: The titration is carried out with a quantitative copper sulphate solution made to contain 0.4 per cent of copper sulphate (0.004 gm. per c.c.). The content of copper is determined exactly by electrolysis. Before titration the specimens are acidified with concentrated sulphuric acid. Copper ferrocyanide is an insoluble red salt but is less insoluble than the well-known Prussian blue. This fact is used in determining the end point of the titration. Drops of concentrated ferric chloride solution are placed on a tile and as the titration proceeds, a drop of the unknown solution is placed in contact with the ferric chloride. If free ferrocyanide is present, an immediate formation of Prussian blue occurs; if all the ferrocyanide has been precipitated as cupric ferrocyanide, a distinct delay occurs in the appearance of this blue color on the tile. The more insoluble ferri-ferrocyanide slowly replaces the slightly more soluble cupric ferrocyanide. The end point is therefore read when the appearance of blue is delayed appreciably (five seconds), and the number of cubic centimeters of copper sulphate required is noted.

If hematuria exists during the period of ferrocyanide elimination the method of titration must be modified, for the sulphuric acid apparently liberates sufficient ferric ions from the hemoglobin to precipitate Prussian blue and thus prevent the formation of the red cupric

ferrocyanide. This difficulty is readily avoided by determining the volume of the specimen of urine, bringing it to a quick boil, which precipitates the protein, and then filtering it. A measured quantity of this filtrate is then acidified with concentrated sulphuric acid and titrated in the usual way, the results being corrected to the original volume of the specimen.

Sodium ferrocyanide, in doses of 0.5 gm., of the hydrated salt (0.25 gm. of anhydrous sodium ferrocyanide) has been used in more than 100 individuals for the purpose of studying the glomerular efficiency.

It has proved entirely nontoxic in this dosage, when slowly administered intravenously.

The normal secretion curve is characteristic and shows but relatively little spread of variation. This variation is less than that of phenolsulphonphthalein excretion.

So far as is known, ferrocyanide salts are excreted solely by way of the glomeruli.

In hypertensive arterial disease the excretion of ferrocyanide is considerably retarded, much more so than the phenolsulphonphthalein elimination.

In congestive heart failure both the phenolsulphonphthalein and the ferrocyanide elimination are impaired.

In known glomerulonephritis the excretion of sodium ferrocyanide is either nil in severe cases or else very much reduced.

This test offers notable potentialities of clinical usefulness, since it is specific for the glomeruli, is safe, is simple of execution, and is quite constant in the normal.

In physiologic investigations of the mechanism of renal secretion the procedure should also prove of considerable value.

Much further work is required before the full significance and import of these studies are understood. The authors hope that this preliminary report may encourage others to extend and amplify this work; it has been their object merely to present a new method and to point out some of its potentialities.

TRICHOMONAS VAGINITIS, Treatment of, With Concentrated Salt Solution, Rosenthal, L., Schwartz, L. S., and Kaldor, J. J. A. M. A. **105**: 105, 1935.

Vaginal douching with 25 per cent salt solution is proposed for the treatment of trichomonas vaginitis.

The principle of the treatment is based on the osmotic effect of concentrated salt solution on *Trichomonas vaginalis.*

The method is nonirritating, simple and inexpensive and can easily be carried out by the patient at home.

The method gives prompt relief from the itching and irritating vaginal discharge and prevents in most cases the recurrence of trichomonas vaginitis.

LYMPHOGRANULOMA INGUINALE, New Immunologic Reaction for, Reiss, F. Arch. Dermat. & Syph. **31**: 215, 1935.

Blood was taken from patients with clinically typical cases verified by a positive Frei reaction. The serum was separated, mixed with a 0.5 per cent solution of phenol and kept in the ice box. Before the test was attempted the serum was proved to be sterile culturally. The experiment was carried out in only six cases, but the results were so uniform that Reiss decided to publish them. On each patient tests were made with the following preparations: (1) the control a 0.5 per cent solution of phenol in physiologic solution of sodium chloride; (2) the Frei antigen; (3) a mixture of 0.05 c.c. of Frei antigen with 0.05 c.c. of blood serum from a patient with lymphogranuloma inguinale (injected intradermally), and (4) 0.1 c.c. of blood serum from a patient with lymphogranuloma inguinale (injected intradermally).

Observations on the reactions revealed that: (1) The reaction to the control solution is negative. (2) The Frei antigen produces a typical infiltrated papule the size of a pea with an erythematous area as large as 1 cm. in diameter. (3) The mixture of Frei antigen and serum causes a somewhat increased reaction as compared with the Frei antigen alone. (4) The reaction to the serum is similar to that to the Frei antigen, i.e., a distinct papule with an erythematous zone.

The reaction to the serum reaches its height in forty-eight hours and disappears in from eight to ten days. Control experiments of the same order carried out on a number of patients (syphilitic and rheumatic) have always given negative results.

From these observations it appears that the blood serum of patients with lymphogranuloma has antigenic properties. The increased reaction to the combination of antigen and serum is probably an accumulative effect.

BONE MARROW: Sternal Marrow Aspirated During Life, Young, R. N., and Osgood, E. E. Arch. Int. Med. **55**: 186, 1935.

The technic of sternal puncture found to be most satisfactory is as follows: With the patient lying on his back, with his chest elevated by a pillow beneath his shoulders, the region of the sternomanubrial junction is prepared with iodine and alcohol. Using aseptic technic, the sternomanubrial junction is located as a distinct ridge opposite the sternal cartilages of the second ribs, and the skin, the subcutaneous tissues and the periosteum of the region are infiltrated with procaine hydrochloride. Using an 18 gage spinal puncture needle, from 3 to 4 cm. in length, the sternomanubrial junction is entered in the midline at an angle of about 60 degrees to the surface of the chest. Then the needle is depressed to an angle of about 30 degrees and is forced into the marrow cavity of the body of the sternum, care being taken not to exceed a depth of 1.5 cm. If much resistance is encountered, the needle is rotated while pressure is maintained to facilitate penetration. The stylet is then removed, and, using a 2 c.c. Luer syringe, 1 or 2 c.c. of marrow is aspirated. If no marrow appears after strong aspiration, the stylet is replaced, the needle is inserted a little deeper and aspiration is done. Then remove the syringe from the needle and transfer the aspirated material, which looks like blood, into a 4 × ½ inch (10.16 by 1.27 cm.) test tube containing from 2 to 4 mg. of powdered potassium oxalate, shaking well to insure mixing. The stylet is then replaced, the needle is withdrawn and the puncture wound is sealed with collodion.

The oxalated marrow can be used for any type of hematologic examination which can be done on oxalated blood.

BLOOD: Hemoglobin and Red Cell Content in Normal Women During Successive Menstrual Cycles, Leverton, R. M., and Roberts, L. J. J. A. M. A. **106**: 1459, 1936.

The hemoglobin and red cell content of the blood of four normal women on a constant diet was determined almost daily for three months. Analysis of the data shows the occurrence of daily variations in both hemoglobin and red cells, the majority of which are not greater than the experimental error. The standard deviation for the entire series is 0.9 gm. for hemoglobin and 0.31 million for red cells.

There was a definite upward trend in the hemoglobin values of every subject during the entire period. The values increased from 12.95, 12.54, 11.62 and 13.06 gm. per hundred c.c. for subjects A, B, C and D respectively for the first menstrual cycle to 14, 13.92, 13 and 14.3 gm. for the last cycle in the study. There is a possible significance of these increases, since they suggest a storage of measurable amounts of iron from a diet containing only the usual standard recommendation for this mineral but well fortified in other dietary essentials.

BLOOD SEDIMENTATION As an Aid in Differentiating Acute Appendicitis and Acute Salpingitis, Watson, A. Am. J. M. Sc. **189**: 383, 1935.

In a study of 19 cases of acute salpingitis and 38 cases of acute appendicitis, there is a definite suggestion that the sedimentation time may be of some value in differentiating these two conditions, if the duration of symptoms when the test is made is taken into consideration. During the first twenty-four or even forty-eight hours after the onset of symptoms, the sedimentation time is apt to be shorter in acute salpingitis than in acute appendicitis; an occurrence that is not unfailing but frequent enough to be given consideration, as it is more uniform than either the leucocyte count or the differential.

In accounting for this difference in the behavior of the sedimentation time in the two conditions, there can be no assumption that the difference in the infecting organism can be a

factor. It may, however, be due to difference in the two organs as regards their function and nerve supply. The appendix is supplied by both sympathetic and parasympathetic nerve fibers. Gastrointestinal symptoms occur for some time before there is any tenderness localized over the region of the appendix. Furthermore the appendix is a vestigial organ which is capable of only slight distensibility before it begins to cause symptoms. The fallopian tube has only sympathetic nerve fibers, it is a functioning organ which is capable of relatively great distensibility before causing symptoms. It is shown that with the duration of the infection the sedimentation time becomes shortened in the case of acute appendicitis, and it may be inferred that this is probably what happens in acute salpingitis. But in the case of salpingitis, the infection progresses further before giving symptoms. Therefore, the sedimentation time in acute salpingitis is shorter in the first twenty-four and forty-eight hours after onset of symptoms, because the infection has been there many hours before it begins to cause symptoms.

The red cell count remained remarkably constant for all subjects throughout the experiment. In one case when 5 mg. of iron from ferric ammonium citrate was given daily during two menstrual cycles the red cell content increased 0.5 million per c.mm. and the hemoglobin content increased 1 gm. per hundred c.c. These higher values were not maintained when the citrate was discontinued.

From the data it appears that there is no definite or consistent measurable effect of the process of menstruation on the daily values of either hemoglobin or red cells in the subjects studied. Although occasional marked daily variations in the blood values occur, they do so irrespective of the different phases of the menstrual cycle.

The results of this study emphasize the fact that the existence of normal daily variations in hemoglobin and red cell count, even in subjects under controlled conditions, must be recognized when one judges the significance of single determinations or the influence of the menstruation process on these blood constituents.

AGRANULOCYTOSIS, Pathological Changes in Bone Marrow in, Darling, R. C., Parker, F., Jr., and Jackson, H., Jr. Am. J. Path. 12: 1, 1936.

The uniformity of the pathologic changes in the bone marrow suggests that agranulocytosis is probably a disease entity.

Rapidly fatal cases show lack of maturation in the granular series and hyperplasia of the stem cells.

Cases where death took place after a longer period usually show hypoplasia of myeloid tissue with the coincident appearance of many plasma cells and lymphocytes.

In no case were there obvious changes in the red blood cell series, or any degenerative changes in the white blood cell series.

The recovery stage is characterized by rapid development of the stem cells into myelocytes, metamyelocytes and polymorphonuclear neutrophiles, a sequence of events which would appear to substantiate Fitz-Hugh and Krumbhaar's and Custer's contention of a maturation arrest.

For this maturation arrest is suggested the term "granulocytic" anakmesis.

RADIUM POISONING, Experimental, Rosenthal, M., and Grace, E. J. Am. J. M. Sc. **191**: 607, 1936.

The general features of radium poisoning as observed in human cases have been reproduced in rabbits by oral administration of radium sulphate.

Jaw necrosis, a characteristic of the early acute cases among radium dial painters, can be produced experimentally by radium alone without mesothorium.

In the bone marrow striking changes are produced, consisting of an early hyperplasia of the erythropoietic elements followed by a decreased maturation of the erythroblasts and the replacement of these elements by myelocytes. Finally this hyperplastic marrow is replaced by fibrous tissue.

In the lymph nodes there is noted an initial stimulation of the stem cells with subsequent damage to these cells, resulting in depletion and atrophy of the lymphoid tissue. In the circulating blood an absolute lymphopenia is found.

The development of myeloid tissue in lymph nodes and spleen associated with the extreme myelocytic hyperplasia in the marrow of our animals suggests that the occurrence of leucemia in roentgen ray and radium workers may not be a pure coincidence.

PNEUMONIA, Dose of Antibody Effective in the Treatment of Pneumococcus Type II, Finland, M., and Dowling, H. F. Am. J. M. Sc. **191**: 658, 1936.

Clinical attempts to determine the proper dose of serum in the treatment of cases of pneumococcus Type II pneumonia have emphasized the importance of having a uniform standard with which the potency of various lots of Type II antipneumococcus serums can be compared. The adoption of an international standard, as proposed by Hartley and Smith, is highly recommended.

A tentative plan of dosage for Type II cases is offered, which is based upon observations on the effect of various amounts of antibody:

1. When a diagnosis of Type II pneumococcus pneumonia is made, an amount of Type II antibody equivalent to 100,000 or, preferably, 150,000 units of the proposed standard serum should be given to the patient in as short an interval as is consistent with the avoidance of untoward reactions.

2. An additional 200,000 units should be given to all cases showing Type II pneumococci in the blood culture. This amount should also be given in as short an interval as is consistent with safety and even in spite of apparent improvement in the patient's condition.

3. Additional amounts of 50,000 to 100,000 units should be given at intervals of six to twelve hours in all cases until the fever and other acute symptoms are relieved, or until it is shown that these symptoms are not due to the Type II pneumococcus pneumonia.

4. After treatment is once begun, it is unwise to permit an interval of more than twelve hours to elapse without giving further serum, unless the patient is relieved of fever and serious symptoms.

Treatment with antibody beginning after the end of the fourth day of illness is probably of no benefit, except possibly in nonbacteremic cases, and then only if it is begun during the fifth day.

The results of blood cultures are the most important guide to serum disage, in addition to being of great prognostic significance.

The interests of physician and patient are served if only serums of high potency in Type II antibody are released for treatment of patients with pneumonia due to this type.

BR. ABORTUS, Recovery of, From the Stools of Healthy Carriers, Goldstein, J. D., Fox, W. W., and Carpenter, C. M. Am. J. M. Sc. **191**: 712, 1936.

Brucella abortus was recovered from 2 of 219 stools obtained from patients who were not suspected clinically of having undulant fever.

Guinea pig inoculation of the stool sediments was substituted for the plate culture method of Amoss and Poston.

Brucella abortus, when mixed with human feces and stored at 8° C., remained viable for at least 150 days.

REVIEWS

Books and Monographs for Review should be sent direct to the Editor, Dr. Warren T. Vaughan, Professional Building, Richmond, Va.

Toxicology, or the Effects of Poison*

THIS volume, essentially a didactic text, has been revised and, where necessary, rewritten to include the newer advances since the last edition.

Among the subjects not previously included are avertin, camphor substitutes, mercurial diuretics, the newer barbituric acid derivatives, quinine and its substitutes, triorthocresyl phosphate, and thyroid.

Among the sections which have been largely rewritten are those on carbon tetrachloride, thymol, thallium, and food poisoning.

Concise yet comprehensive this excellent little book will doubtless receive the same favorable reception accorded to the two previous editions.

It can be recommended as an authoritative text.

The Harvey Lectures†

THIS volume contains the following lectures delivered under the auspices of the Harvey Society of New York. The Etiology of Pernicious and Related Macrocytic Anemias, by William B. Castle. This is a presentation of controlled experimental production and relief of macrocytic anemia, induced by varying the three potential causative factors: the extrinsic factor, contained in food; the intrinsic factor, produced in the stomach; and the adequate absorption of products of digestion through the upper gastrointestinal tract. The Significance of the Amino Acids in Nutrition, by William C. Rose, is the publication of recent evidence gathered from an attempt to isolate the unknown indispensable growth stimulating and maintaining factor which is a part of protein food. The Present Geographic Distribution of Yellow Fever and Its Significance, by Wilbur A. Sawyer, is a report of surveys that have been conducted throughout the world, with special emphasis on the endemic areas of Africa and South America. There are statistics which throw new light on the epidemiology of, and immunity to, yellow fever. Urine Formation in the Amphibian Kidney, by A. N. Richards. In this remarkable paper there is a description of experimental procedures carried out on the kidney of the frog and necturus. By means of micropipettes the author collected pure glomerular filtrate and samples of urine from various levels of the kidney tubules. His analyses, compared with analysis of plasma, add direct proof to the theory of simple glomerular filtration, rather than glomerular secretion, and absorption of threshold substances in the tubules. A Study of Specificity in Relation to Hormone and other Biological Relations, by E. C. Dodds. This is a report of the preparation of a group of synthetic estrin-producing substances; the results of his experimentation point toward the fact that there is very little specificity in hormone production. Circulation in Striated and Plain Muscles in Relation to Their Activity, by G. V. Anrep, is a discussion of vasodilatation in the contracting muscle, and presentation of experimental evidence which tends to disclose its mode of initiation. Artificial

*Toxicology, Or The Effects of Poisons. By F. P. Underhill. Third Edition revised by Theodore Kappanyi, Professor of Pharmacology and Materia Medica, Georgetown University Medical School. 325 pages, Cloth. P. Blakiston's Son & Co., Philadelphia, Pa.

†The Harvey Lectures. Delivered under the auspices of The Harvey Society of New York. 1934-1935. Under the patronage of the New York Academy of Medicine. By Dr. Wm. Bosworth Castle, Dr. Wm. Cumming Rose, Dr. Wilbur A. Sawyer, Dr. Alfred N. Richards, Dr. E. C. Dodds, Dr. G. V. Anrep, Dr. Francis G. Blake, Dr. John H. Northrop. Series XXX. Cloth. Pages 270. The Williams and Wilkins Company, Baltimore, 1936.

Pneumothorax in Lobar Pneumonia, by Francis G. Blake. The author presents a series of cases of lobar pneumonia treated by use of artificial pneumothorax; the group is classified according to the duration of the disease in relation to initiation of the pneumothorax. The results are analyzed. Isolation and Properties of Pepsin and Trypsin, by John H. Northrop, is the concluding paper of this series. The author has prepared crystalline trypsin compounds and studied their structure and pharmacology.

Roentgenographic Technique*

THIS book, a revision of the first edition, is a manual intended for those who use the x-ray for diagnostic purposes. The opening chapters are devoted to discussion of the general physical principles of electricity in its special application to roentgen rays: this is followed by a detailed description of roentgen rays and the various parts of the x-ray equipment. There are a series of experiments for the beginner, devised as a correlation between the physical principles and their actual application, intended to form a rational basis for the various procedures. There are easily comprehended instructions for the development of technic, with special emphasis on the exposure and development of films. The second part of the book is divided into chapters devoted to the special systems of the body in their relationship to x-ray technic. The skeletal system is discussed at length, and in connection there are numerous illustrations representing the relative positions of the tube, the area to be filmed, and the plate. Throughout this section emphasis is placed on the arrangement of tube and plate in such manner that detailed films may be produced with little or no disturbance of the position of the affected part. In connection with the gastrointestinal and genitourinary systems there is presentation of detailed technic for the special procedures required to visualize these organs. This work does not deal with roentgen ray therapy, but is a very complete guide for the x-ray technician.

Laboratory Manual of Physiological Chemistry†

IN THEIR preface the authors announce that this is a revision of the former editions; that the chapter on colloids has been omitted; that minor changes have been made throughout the book; and that several new experiments have been embodied in the chapter devoted to blood. The material is all presented in the form of experiments. Chapter 2 deals with qualitative and quantitative tests for the carbohydrates, demonstrating their various chemical properties. Experiments designed for the recognition and identification of the fats, lipids, and cholesterol are embodied in the next chapter. Chapter 4 is devoted to tests for the proteins and metaproteins by means of physical and chemical means, and for recognition of certain of the amino acids. One chapter is devoted to the quantitative determination of the constituents of milk, bone, and connective tissue. The next section is devoted to the enzymes of the digestive tract, together with the products of digestion. Chapters 7 and 8 describe in detail the necessary steps for the qualitative and quantitative determination of the normal and abnormal constituents of urine and blood. Throughout the work there are complete footnotes devoted to preparation of solutions and details of technique necessary for accurate results. The general arrangement and the bold-faced heading of each experiment simplifies the location of individual material. The authors have presented their material in a concise

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*Roentgenographic Technique. A Manual for Physicians, Students and Technicians. By Darmon A. Rhinehart, A.M., M.D., F.A., G.R., Professor of Roentgenology and Applied Anatomy, School of Medicine, University of Arkansas: Roentgenologist to St. Vincent's Infirmary, Baptist State Hospital, Missouri Pacific Hospital, and the Arkansas Children's Hospital, Little Rock, Arkansas. Second Edition. Thoroughly Revised. Illustrated with 183 Engravings. Cloth. Pages 431. Lea and Febiger, Philadelphia, 1936.

†Laboratory Manual of Physiological Chemistry. By Mayer Bodansky, Director of Laboratories, John Sealy Hospital, Galveston, and Professor of Pathological Chemistry, University of Texas; and Marion Fay, Associate Professor of Biological Chemistry, School of Medicine, University of Texas. Third Edition. Cloth. Pages 258. New York. John Wiley and Sons, Inc., London. Chapman and Hall, Limited, 1935.

yet complete manner and have condensed into a small volume all the necessary material information that is to be found in larger and more expensive works on this same subject. Although this book is intended primarily as a manual for laboratory classes in physiological chemistry, it makes an ideal handbook and reference book for all those engaged in laboratory work in hospitals or offices.

Exophthalmic Goiter and Its Medical Treatment*

THIS volume is an exhaustive study of the condition of Grave's disease, with a consideration of all its aspects. Dr. Bram stresses the fact that exophthalmic goiter is a generalized disease which requires generalized treatment, only one phase of which is local treatment of the thyroid gland. The source from which the material is derived is a series of more than five thousand cases which have come under the author's observation. The type of individual susceptible to the development of Grave's disease, and the emotional shocks which are responsible for its initiation, are discussed. The symptomatology of exophthalmic goiter, in its flagrant and obscure forms, and the variety of ways in which it affects the systems of the body are considered. The author differentiates sharply between toxic adenoma, a local disease of the thyroid gland, and exophthalmic goiter, in which there is a disturbance of all body physiology. There is a detailed discussion of the numerous laboratory tests and procedures, with a consideration of the attributes and variability of each; he emphasizes the fact that they should be used only as supplements to the physical findings, and that they require sane and expert interpretation. The importance of psychotherapy in the treatment is illustrated by numerous examples. He enlarges on the other forms of treatment, which include rest, diet, local treatment of the gland, and surgery when desirable, and presents long lists of indicated and contraindicated drugs. He concludes this exhaustive study of the complete management of a case of Grave's disease with a presentation of a large number of case records, intended to illustrate the wide variation between individual cases, and the specialized treatment required for each.

Essentials of Physiological Chemistry†

THE author in his preface announces that this work is intended primarily for medical students who are being introduced to the field of biochemistry. For that reason, in order to avoid confusion, he has presented his material in concise, somewhat didactic form, and has avoided controversial discussion in connection with the subjects in this field which are as yet not definitely settled. The text comprises all of the important material that may be found in the more voluminous works dealing with this same field. It includes a basic introduction to physiological chemistry, and a chapter devoted to the physical properties of solutions and colloids, which is a condensation of numerous principles of physical chemistry. There are short comprehensive discussions of the carbohydrates, lipids, and proteins, which consider their structures, activities and functions. The subject of food and enzymes is presented next, along with digestion and ferments in the various parts of the gastrointestinal tract. Absorption, colorimetry and metabolism of carbohydrate, fat, and protein are considered. Constituents, normal and abnormal, of the blood and urine are discussed. The closing chapters deal with the hormones of the various endocrine glands and the sources and functions of the vitamins.

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*Exophthalmic Goiter and its Medical Treatment. By Israel Bram, M.D., Medical Director, Bram Institute for the Treatment of Goiter and other Diseases of the Ductless Glands, Upland, Pa.; Formerly Instructor in Clinical Medicine, Jefferson Medical College, Philadelphia; Member of the Association for the Study of Internal Secretions, The American Association for the Study of Goiter, etc. Foreword by R. G. Hoskins, Ph.D., M.D., Director of Research, Memorial Foundation for Neuro-Endocrine Research, Harvard Medical School, Boston, Mass. Second Edition. Completely Revised and Enlarged with 79 Illustrations. Cloth. Pages 456. The C. V. Mosby Company, St. Louis, 1936.

†Essentials of Physiological Chemistry. By Arthur K. Anderson, Ph.D., Professor of Physiological Chemistry, The Pennsylvania State College. Cloth. Pages 257. John Wiley & Sons, Inc., New York, 1935.

The International Medical Annual*

THIS newest edition of the International Medical Annual has been compiled in a manner similar to that employed in the preceding volumes. The same dictionary or encyclopedic form of presentation, which simplifies its use for reference, has been retained. As in former years the Medical Annual is a review of the advances made in the treatment of disease during the preceding year—1935. The contributors are British Physicians and Surgeons; each one is a recognized authority in that phase of medicine or surgery which he reviews for this volume. In their preface the Editors announce that the international literature for 1935 has been exhaustively reviewed, and those articles which seem to present an advance in the modern treatment of disease have been selected. The contributors have extracted the conclusive points, condensed them into a few sentences, and presented them in short paragraphs, heavy with information. Brevity is the keynote of this work, and only those references which present a departure from the usual method of treatment have been included. It embraces discussions of such widely varying subjects as the treatment of lobar pneumonia, advances in thyroid surgery, breech presentation, and diseases of the breast.

The Adrenals†

THIS monograph is perhaps the most complete analysis of the mass of recent investigative work that has been carried out in relation to the adrenal glands. The author groups his work into four subdivisions: Anatomical aspects; the Medulla; the Cortex; and Clinical considerations. He discusses the gross anatomy and histology from a comparative anatomical and embryological approach. The androgenic tissue is considered in detail. The section devoted to the medulla deals with its physiology and the chemistry and pharmacology of epinephrine. The anatomy, physiology, and pathology of the cortex in man and experimental animals, is the subject of the following division. It is a basis for the consideration of the relationship between adrenal function and blood chemistry, metabolism, and the other endocrine glands. A scientific approach to the matter does a great deal to clarify the relation of the adrenals to surgical shock, infection, and immunity. Under clinical considerations there is a thorough discussion of Addison's disease, tumors of the adrenals, and the adreno-genital syndrome which may so easily be confused with conditions which primarily affect the gonads. There seems to be no phase of the anatomy, physiology, and pathology of these organs that has not been studied and presented in this volume in enlightening detail. This work is heartily recommended to those who are interested in the newer advances made in the study of the adrenal glands.

Medical Papers‡

THIS volume, containing 104 papers covering a variety of subjects, is dedicated to Henry Asbury Christian in honor of his sixtieth birthday by his present and past Associates and House Officers at the Peter Bent Brigham Hospital who take this method of demonstrating their gratitude to him while he is still alive and able to appreciate it.

If there were any doubt of Dr. Christian's ability as a teacher and trainer of physicians in the highest sense of the word, it would be resolved by the perusal of this memorial volume. For in the extent and variety of the subject covered as well as the manner of their presenta-

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*The International Medical Annual. A Year Book of Treatment and Practitioner's Index. Editors: H. Letheby Tidy, M.A., M.D., (Oxon.), F.R.C.P., and A. Rendle Short, M.D., B.S., B. Sc., F.R.C.S. 36 Contributors. Fifty-fourth Year. 1936. Cloth. Pages 555. William Wood and Company, Baltimore.

†The Adrenals. By Arthur Grollman, Ph.D., M.D., Associate Professor of Pharmacology and Experimental Therapeutics; and Formerly Associate Professor of Physiology, in the Medical School of The Johns Hopkins University. Cloth. Pages 410. The Williams and Wilkins Company, Baltimore, 1936.

‡Medical Papers, Dedicated to Henry Asbury Christian. The Waverly Press, Baltimore, Md.

tion, the imprint of association with Dr. Christian is apparent on every page. It is impossible to select for specific comment any one or more contributions over others, for all are distinct contributions of interest and value.

Those, and they can be but few, who are somewhat unfamiliar with Dr. Christian's work will read with interest the Introduction by I. C. W. and the Appreciation by W. T. V.

Dr. Christian is numbered for all time among the relatively few whose life and works constitute a milestone in the development of modern medicine and whose influence, as reflected in those fortunate enough to have benefited by association with and training under him.

The Committee, under Dr. Robert T. Monroe, is to be congratulated upon an excellent collection of papers and Dr. Christian upon the affection and respect he has evidently inspired.

The Specificity of Serological Reactions*

AS STATED by the author, the purpose of this book is to review the experiments conducted by himself and his colleagues on antigens and serological reactions with simple compounds as well as to discuss the phenomena of serological specificity, with particular reference to the chemical aspects of immunological reactions.

The chapter sequence broadly corresponds to the development of the subject and covers: The serological specificity of proteins; and the practical applications of serological protein reactions; the specificity of cell antigens; the specificity of antibodies; artificial conjugated antigens and serological reactions with simple chemical compounds; and chemical investigations on specific cell substances; carbohydrates; lipoids.

In addition to the rather extensive bibliography following each chapter a list of the important textbooks, reviews, and monographs on the subject is appended. An index renders the contents of the book accessible.

The reputation of the author in this field assures the reader of a balanced and authoritative discussion of an involved subject and the book will prove of value, not only to the reader not wholly familiar with the subject—for whom explanations of elementary concepts and phenomena of serology are provided—but particularly to the workers in this field who will here find it comprehensively surveyed and authoritatively discussed.

The Cerebrospinal Fluid and Its Relation to the Blood†

THE purpose of this book is to present in an orderly, consecutive, and comprehensive manner the extensive data produced by the investigations of many workers concerning the cerebrospinal fluid and its relation to the blood.

Dr. Katzenelbogen's wide experience and work in this field render him especially suited to this task which he succeeded in carrying out exceedingly well.

The book, while obviously neither a technical manual nor a textbook in the usual sense, will prove of great value as a reference source and as presenting in a systematic manner the wealth of information accruing from the studies of the last two decades.

The first three chapters of the book are devoted to a discussion of the origin, mode of formation, and circulation of the cerebrospinal fluid as such.

The remainder—and by far the greater portion of the book—is given over to a discussion of the studies which have been made of the physico-chemical constitution of the cerebrospinal fluid as compared to that of the blood in various physiological and pathological conditions.

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*The Specificity of Serological Reactions. By Karl Landsteiner, M.D. Cloth, 178 pages, 29 tables. Charles C. Thomas, Springfield, Ill.

†The Cerebrospinal Fluid and Its Relation to the Blood. A Physiological and Clinical Study. By Solomon Katzenelbogen, M.D., Associate in Psychiatry, in charge of The Laboratory of Internal Medicine, The Henry Phipps Psychiatric Clinic, The Johns Hopkins Medical School. Cloth, 468 pages, 46 tables and 20 charts. The Johns Hopkins Press.

In this connection certain therapeutic procedures are discussed in the light of present concepts of the barrier between the blood and spinal fluid, especially as concerns the presence of antibodies, in meningitis, and in relation to arsenotherapy.

To the pathologist, the syphilologist, the pathologist, and the physician alike this book should prove an invaluable reference.

Recent Advances in Medicine*

THIS well-known volume of the equally well-known Recent Advances Series requires no introduction.

This eighth edition of Beaumont and Dodds has been thoroughly and extensively revised and while increased in size by only thirty-five pages, presents, as heretofore, a comprehensive and authoritative review of the recent advances in diagnosis and treatment.

Those familiar with previous editions of this book will welcome the new text while to those heretofore unfamiliar with it, this book will prove of practical and continual value in the elucidation of everyday as well as of the more complex problems encountered in medical practice.

It may be heartily recommended as a practical, useful, and authoritative text.

Textbook of Roentgenology: The Roentgen Ray in Diagnosis and Treatment†

IN THIS book roentgenology is presented in a manner and from a viewpoint somewhat different from the majority of texts upon this subject, which, as a rule, begin with the film and work backward toward the underlying pathology.

Dr. Harrison begins with the pathology and then discusses roentgenology as applied, not only to diagnosis, but also, when possible, to the treatment of the particular lesion. For this reason this book should prove of interest and value to the clinician as well as the roentgenologist.

The roentgenologist must naturally be regarded as primarily a consultant. Unfortunately, the clinician not infrequently associated the roentgenologist more or less with the film and, consequently, too often requests "an x-ray of the chest" without further specification, and without, perhaps, always a clear conception of just what the x-ray appearance of varied lesions may be. On the other hand, the roentgenologist sometimes reports "haziness" and so on without any clear suggestion as to its cause.

The purpose of this book is to emphasize that a consultant in the true sense of the word, as is true of a consultant in any field, must be somewhat of a pathologist.

It will, without doubt, be surprising to many clinicians and even, perhaps, to some roentgenologists, to learn from this book that pathological lesions of varied kinds show more or less suggestive appearances. Certainly this book should be well received by both clinician and pathologist as bringing each in closer touch with the other's angle of view of the particular problem with the solution of which they are mutually concerned.

To the clinician this book should prove of special interest and value because of its presentation and discussion of the various conditions amenable to treatment with x-rays, a subject upon which there is certainly some confusion, not all of it clinical. Both clinician and roentgenologist will be interested in the comprehensive discussion of the effect of radiation upon normal tissues.

All in all, this is a book with a distinctly new viewpoint and a distinct field of usefulness. It can be recommended to clinician, roentgenologist, and pathologist alike as an excellent and useful reference text.

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*Recent Advances in Medicine, Clinical, Laboratory, Therapeutic. By G. E. Beaumont, M.D., and E. C. Dodds, M.D. Edition 8, 450 pages, 46 illustrations, Cloth. P. Blakiston's Son & Co., Inc., Philadelphia, Pa.

†A Textbook of Roentgenology. The Roentgen Ray in Diagnosis and Treatment. By Bede J. Michael Harrison, Director of Department of Roentgenology, Vancouver General Hospital, etc. Cloth, 826 pages, 238 figures. William Wood & Co., Baltimore, Md.